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Neural correlates of context-dependent memory: The role of the insula in episodic encoding and recognition memory – an fMRI experiment

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Mein Dank gilt meinen Eltern,
Karola & Ronald Campe,
welche mir vom ersten Tag an
alles haben möglich gemacht

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Das experimentelle Paradigma des „Scheiterns der Wiedererkennung wieder erkennbarer Wörter“ (recognition failure of recognizable words; Tulving & Wisemann, 1975; Gardiner, 1994) wurde für die funktionelle Magnetresonanztomographie adaptiert und dient als neuer Ansatz zur Untersuchung episodischen Gedächtnisses. Die Analyse der Enkodierungs- und Wiederabrufsaktivität bietet die Möglichkeit Aktivitätsmuster zu untersuchen, die kontextabhängige und kontextunabhängige subsequente Gedächtnisinhalte sowie Erfolg und Misserfolg des Wiederabrufs abbilden. Die Ergebnisse der Wiederabrufdaten weisen auf ein Aktivitätsmuster innerhalb des MTL hin, welches zwischen wiederabrufsbaren und nicht wiederabrufbaren Zielwörtern unterscheidet, jedoch nicht mit kontextabhängigem Gedächtnis assoziiert ist. Kontextabhänigigkeit im Rahmen des Verhaltenseffekts konnte für die bilateralen anterioren Inselkortices (AIC) gezeigt werden. Interferenz mit der Wiederabrufprozessierung, die ihren Ausgangspunkt in der bilateralen AIC nimmt, kann auch den Effekt des „Recognition failure of recognizable words“ erklären.

Eine zweite Fragestellung untersucht Aktivitätsmuster bei kontrollierter und automatischer Wiedererkennung. Sie bestätigt die Hypothese des „Attention-to-Memory-Model“ (Ciaramelli et al., 2008) und liefert zusätzliche Daten, die auf unterschiedliche Aktivitätsmuster innerhalb kortikaler Konnektivitätsnetzwerke hinweisen. Der Wechsel zwischen dem Default-mode-Netzwerk bei automatischer und dem zentralen Exekutivnetzwerk bei kontrollierter Wiedererkennung wird durch die AIC bei Präsentation des jeweiligen Hinweiswortes induziert (siehe auch Sridharan et al., 2008).

Zusammenfassung

Das experimentelle Paradigma hinter dem Verhaltensphänomen des „Scheiterns der Wiedererkennung wieder erkennbarer Wörter“ (recognition failure of recognizable words; Tulving & Wisemann, 1975; Gardiner, 1994) wurde für die funktionelle Magnetresonanztomographie adaptiert. Während die meisten anderen Paradigmata das Gedächtnis für die Kontextinformation selbst messen, z.B. Erinnerung und Vertrautheit (Recollection und Familiarity) sowie Quellgedächtnis und Begriffsgedächnis (source-memory und item-memory), bestimmt dieses Paradigma einen eher zufälligen Einfluss einer Kontextmanipulation auf episodische Gedächtnisenkodierung und Wiederabruf. Dieser Ansatz könnte damit eine neue Herangehensweise sein, episodisches Gedächtnis mit Hilfe von funktioneller Bildgebung darzustellen.

Die Analyse der Enkodierungs- und Wiederabrufsaktivität während der drei Akquisitionsphasen bietet die Möglichkeit Aktivitätsmuster zu untersuchen, die kontextabhängige und kontextunabhängige subsequente Gedächtnisinhalte sowie Erfolg und Misserfolg des Wiederabrufs abbilden. Das Hauptinteresse der Untersuchung galt dem Phänomen des „Scheiterns der Wiedererkennung wieder erkennbarer Wörter“. Basierend auf den Annahmen des BIC Models (Bindung von Item und Kontext; Diana et al., 2007) wurden neuronale Korrelate in der Umgebung des medialen temporalen Lobus (MTL) vermutet. Die Ergebnisse der Analyse unterstützen diese Hypothese jedoch nicht vollkommen. Während der Enkodierungsphase wurde keine Aktivität im MTL detektiert (zum Vergleich Henson, 2005). Die Ergebnisse der Wiederabrufdaten weisen auf ein Aktivitätsmuster innerhalb des MTL hin, welches zwischen wiederabrufsbaren und nicht wiederabrufbaren Zielwörtern unterscheidet. Dies gilt sowohl für kontextabhängigen als auch für kontextunabhängigen Wiederabruferfolg versus Vergessen. Daraus lässt sich schlussfolgern, dass in diesem Paradigma der MTL nicht mit kontextabhängigem Gedächtnis assoziiert ist. Stattdessen zeigte ein anderes neokortikales Areal Aktivität für Kontextabhänigigkeit im Rahmen des Verhaltenseffekts – die bilateralen anterioren Inselkortices (AIC). Die AIC war beim Enkodieren und während des ersten Wiedererinnerungstests (andere Kontextbedingung) in unterschiedlichem Maße aktiv für kontextabhängige im Vergleich zu kontextunabhängigen und vergessenen Zielwörtern. Während des zweiten Wiedererinnerungstests (gleiche Kontextbedingung) verringerte sich die Aktivität in der AIC mit zunehmender Exposition und bewusster Verarbeitung des Wortpaares durch den Probanden (vergessene > kontextabhängige > kontextunabhängige Zielwörter).

Craig (2009) postulierte einen formativen Einfluss der AIC in der Entstehung des Bewusstseins und der Selbstwahrnehmung. Die ROI-Analyse (region of interest) der AIC in

der Enkodierungsphase deutet auf eine Verbindung zwischen Zielwort und Kontext hin, welches ein Hinweis auf eine starke Verbindung zwischen dem menschlichen Bewusstsein und der Langzeitgedächniseinspeicherung sein könnte. Das bewusste Empfinden jedes einzelnen jeweils gegenwärtigen Zeitpunktes könnte in manchen Situationen durch Interferenz mit der Wiederabrufprozessierung auch den Effekt des „Recognition failure of recognizable words“ erklären. Die bilaterale AIC scheint die Ursache dieser Interferenz zu sein.

Darüber hinaus erlaubt diese Studie die Untersuchung einer zweiten Fragestellung, welche sich mit kontrollierter und automatischer Wiedererkennung beschäftigt. Kontrollierte Wiedererkennungsprozesse sind nötig um die Abweichung zwischen neuem Wiedererkennungshinweis und enkodierter Information während des ersten Wiedererkennungstests aufzulösen (andere Kontextbedingung). Wird der enkodierte Inhalt erneut präsentiert (gleiche Kontextbedingung) ist ein automatischer Wiedererkennungprozess ausreichend um die gelernte Information abzurufen. Das „Attention-to-Memory-Model“ (Ciaramelli et al., 2008) verweist auf Aktivität in unterschiedlichen parietalen Kortexarealen bei Wiedererkennung unter gleichen Kontextbedingungen im Vergleich zu Wiedererkennung unter anderen Kontextbedingungen. Diese Hypothese wird durch einen Interaktionseffekt zwischen den Wiedererkennungstests bestätigt. Das parietale Areal, welches mit „Top-down attention to memory“ assoziiert ist, wird bei kontrollierter Wiedererkennung aktiv. Dieser Effekt liefert zusätzliche Daten, die auf unterschiedliche Aktivitätsmuster innerhalb kortikaler Konnektivitätsnetzwerke hinweisen. Bei kontrollierter Wiedererkennung werden Areale aktiviert, die mit dem zentralen Exekutivnetzwerk assoziiert sind (CEN; Eckert et al., 2009; Menon & Uddin, 2010), dies beinhaltet auch die bilaterale AIC. Wiedererkennungsprozesse von Gedächnisinhalten werden vielfach mit dem Default-mode-Netzwerk assoziiert (DMN; Menon & Uddin, 2010; Raichle et al., 2001; Maguire, 2001a). Jedoch könnte das zentrale Exekutivnetzwerk Wiedererkennungprozesse unterstützen, wenn das präsentierte Hinweiswort nicht zu automatischer Wiedererkennung der enkodierten Information führt (Badre & Wagner, 2002; Bressler & Menon, 2010). Übereinstimmend mit bisheriger Forschung zu kortikaler Konnektivität legen die Daten dieser Studie nahe, dass automatische Wiedererkennung durch das DMN erreicht wird, während kontrolliertes Wiedererkennen abhängig vom CEN ist (Menon & Uddin, 2010). Der CEN ist jedoch nur einer von zwei Aufmerksamkeitsnetzwerken (Eckert et al., 2009). Das zweite Aufmerksamkeitsnetzwert, das Salience-Netzwerk, wird abhängig von der subjektiven Bedeutung eines Stimulus aktiviert (Seeley et al., 2007). Das Kernareal des Salience-Netzwerkes wird durch die AIC repräsentiert, wo Aktivität vor allem bei kontrollierten Wiedererkennungsprozessen detektiert wird. Sridharan et al. (2008) kamen zu dem Schluss, dass die AIC die Umschaltung zwischen dem DMN und CEN induziert. Die

vorliegende Studie unterstützt diese Aussage, indem sie zeigt, dass die Umschaltung zwischen den Netzwerken durch das präsentierte Hinweiswort ausgelöst wird.

Zusammenfassend lassen die vorgestellten Daten vermuten, dass der AIC eine zentrale Rolle beim Zusammenspiel unterschiedlichen kognitiven Prozessen zukommt. Zu diesen Prozessen gehören Aufmerksamkeit, Bewusstsein und episodisches Gedächtnis.

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List of Abbreviations

AIC	anterior insular cortex
aPFC	anterior prefrontal cortex
BA	Brodmann area
c	response criterion
CEN	central executive network
d’	d-prime
DMN	default mode network
DLPFC	dorsolateral prefrontal cortex
FAR	false alarm rate
HH	hit-hit items
HM	hit-miss items
HTR	hit rate
MTL	medial temporal lobe
MH	miss-hit items
MM	miss-miss items
PFC	prefrontal cortex
VLPFC	ventrolateral prefrontal cortex

1. Abstract

The experimental paradigm behind the behavioral phenomenon of recognition failure of recognizable words (Tulving & Wiseman, 1975; Gardiner, 1994) was adapted for functional magnetic neuroimaging. While the majority of imaging paradigms measure memory for context information (i.e. recollection versus familiarity or source memory versus item-memory), this paradigm assesses a more incidental influence of context on episodic encoding and retrieval. This novel approach may guide imaging of episodic memory into a so far largely unexplored direction.

The acquisition of encoding and retrieval activity over the course of 3 scanning sessions provided the opportunity to analyze activity patterns for contrasts of context-dependent and context-independent subsequent memory, retrieval success, and retrieval failure. On the primary interest of the recognition failure of recognizable words phenomenon; neuronal correlates were hypothesized to be located in the vicinity of the medial temporal lobe (MTL) based on the assumptions of the BIC model (binding of item and context; Diana et al., 2007). However, the data did not support this claim fully. No MTL activity was found during encoding (see also Henson, 2005). The retrieval data suggested an activity pattern within the MTL that differentiates between retrievable targets and irretrievable targets, indicating both context-dependent and context-independent retrieval success versus forgetting. Consequently, the MTL did not appear to be involved with context-dependent memory processes in this paradigm. Instead, another neocortical area demonstrated strong effects for context-dependency leading to the behavioral effect – the bilateral anterior insular cortex (AIC). The AIC was differentially active for context-dependent items compared to context-independent and forgotten items during encoding and the first recognition test (different context condition). During the second recognition test (same context condition), AIC activity decreased with increased exposure and conscious processing of the word-pairs (forgotten > context-dependent > context-independent items).

Craig (2009a) proposed a formative role of the AIC in self-awareness. At encoding, a region of interest analysis of AIC activity suggested a binding of target and context property, hinting towards a strong connection between human consciousness and an episode encoded into long-term memory. The conscious experience of any present moment in time may in some situations also cause the recognition failure of recognizable words effect through interference with retrieval processing. Although, MTL activity patterns and the subsequent memory test confirmed the target's presence in long-term memory, the conscious processing of the external retrieval episode that initiated the retrieval attempt disrupted the post-retrieval

processing leading to recognition failure of recognizable words. The bilateral AIC was the areas implicated in causing this interference.

The present study allowed for a secondary line of questioning focusing on controlled versus automatic retrieval operations. Controlled retrieval processes were necessary to overcome the mismatch between retrieval cue and encoded information in the different context condition (novel context and target); in the same context condition (original context and target), automatic retrieval was sufficient to complete recognition. Differential parietal areas were expected to be active during retrieval in the different context condition compared to retrieval in the same context condition as predicted by the AtoM model (Attention-to-Memory Model; Ciaramelli et al., 2008). Confirming this hypothesis, the parietal clusters found in an interaction effect between retrieval tests indicate top-down attention to memory in the different context condition (controlled retrieval). The same contrast yielded additional data indicating a difference in activity patterns within cortical connectivity networks. For controlled retrieval, areas associated with the central executive network (CEN; Eckert et al., 2009; Menon & Uddin, 2010) including the bilateral AIC were preferentially active. Although, memory retrieval processes are commonly associated with activity in the default mode network (DMN; Menon & Uddin, 2010; Raichle et al., 2001; Maguire, 2001a), under certain circumstances the CEN may have aided retrieval when the presented retrieval cue did not lead to automatic recovery of the encoded information. In accordance with cortical connectivity research, the synopsis of all available data of the present study suggested that automatic retrieval was accomplished by the DMN, while controlled retrieval depended on CEN processing. The CEN is but one of two attentional networks (Eckert et al., 2009). The second attentional network – the salience network – is active depending on the personal salience of stimuli (Seeley et al., 2007). A core area of the salience network is represented by the AIC, with AIC activity preferentially found for controlled retrieval. Sridharan et al. (2008) suggested that the AIC also causes the switch between DMN and CEN. The present study found CEN activity in the different context condition, while DMN activity was acquired in the same context condition for retrieval success, respectively. As a result, this study demonstrated that for episodic memory retrieval the switch associated with the AIC occurred depending on the retrieval cue presented.

In conclusion, the present data strongly suggested that the AIC played a vital and central role in several different cognitive processes and their interaction among each other: attention, consciousness and episodic memory.

2. Introduction – Literature Review

This literature review will present prevalent theories of episodic memory by characterizing encoding, outlining subtypes of retrieval processes as well as presenting alternative models of memory. To understand how episodic memory works, context and the behavioral effect of context manipulations are examined to prepare for an alternative approach to context imaging. Conventional approaches to episodic memory imaging are summarized and common activation patterns in the medial temporal, parietal and frontal lobe are examined. Finally, the so far largely behavioral approach of measuring context-dependent memory is transposed to functional magnetic imaging to uncover neural correlates of context-dependent memory.

2.1. Episodic Memory

Human memory is not a unified concept, but a collection of processes quite distinct from each other. In a broad sense, long-term memory may be separated from short-term memory and is in turn classified as declarative (explicit) or non-declarative (implicit) long-term memory. While explicit memory is consciously experienced, implicit memory remains unconscious. Neuropsychological evidence suggests that declarative memory might not be a unitary process either. Further separation of explicit memory into episodic and semantic was first suggested by Endel Tulving (1972). He proposed that semantic memory supports general knowledge of the world independent of a particular personal event connected to it, while episodic memory is essentially linked to a distinctive individual episode. “The essence of this type of memory is its specificity, its capacity to represent a specific event and to locate it in time and space,” (Baddeley, 2001, p. 1346). Later on, Tulving specified the term further by underlining the “autonoetic” quality of episodic memory – a long-term memory system supporting self-awareness. This unique feature enables us to not only consciously experience one’s own presence but also mentally move between ones past, the present, and even an imaginary future. “Episodic memory does exactly what other forms of memory do not and cannot do—it enables the individual to mentally travel back into her personal past,” (Tulving, 1998, p. 266).

2.2. Encoding and Retrieval

Encoding and retrieval are two essential aspects of any type of declarative memory. For episodic memory – during the learning episode – a specific item and its surrounding context are encoded into the declarative long-term memory system. An encoded episode is essentially any moment in time that may be remembered later on, e.g., meeting a new person or parking the car in the morning. At retrieval, the encoded episode may be remembered through various recall or recognition operations, e.g. recalling where the car was parked, one's first day at school, or recognizing a person one passes on the street.

2.2.1. The Encoding Specificity Principle

Wiseman & Tulving (1976) proposed a theory of encoding success in relation to retrieval. When an item is encoded into memory, contextual information or cues are always encoded with it. They stated that memory performance is best, when the cues or context provided at recall are the same as those present at encoding. Thus, retrieval is most successful if the information provided for the task matches the properties of the encoding event. Tulving (1974) also proposed two types of forgetting. If encoding fails and no memory trace is created, there is no memory to be accessed leading to trace-dependent forgetting. The second kind of forgetting occurs when an item has been encoded successfully but a given retrieval attempt remains unsuccessful. He termed the event when an item is stored in memory but cannot be accessed as cue-dependent forgetting. According to the encoding specificity principle, it is therefore necessary to present an appropriate cue - a cue processed at encoding – for successful retrieval.

2.2.1.1. Testing the Encoding Specificity Principle

There are several classical experiments testing the encoding specificity principle. Thompson & Tulving (1970) presented participants with pairs of words in which the first word was the cue and the second the target. Some of the cues were weakly associated with the target (e.g. Train – BLACK) and some provided a strong association (e.g. White – BLACK). During recall, they tested for targets by providing either a strong or a weak cue (e.g. Train – ?). Any changes from encoding cue to retrieval cue lowered recall. Even changing from a weak encoding cue to a strong retrieval cue lowered performance.

Another related phenomenon to the encoding specificity principle is context change. Godden & Baddeley (1975) set up a remarkable experiment in which they tested the influence of environmental context change on memory performance. In four conditions divers

of the university's diving club studied words presented orally either on land or under water followed by a free recall test in one of the two conditions. As a result, participants learned and recalled words in either the same condition (land – land; water – water) or in a mismatched condition (land – water; water – land). Regardless of where encoding took place, recall suffered if the context (land or water) in the retrieval session did not match the study phase. There was no significant difference in performance between the land – land and water – water conditions or between the land – water and water – land set-up. Differential rehearsal and a disruption by moving from one environment to another might have led to the differential result for the context change groups compared to the same context groups. This alternative explanation for the divergence was addressed in a second experiment. Participants in the land – land condition were required to enter the water and dive in the four minute intermission period. No significant change in results from the original paradigm could be detected, hence, the disruption hypothesis and differential rehearsal were ruled out.

2.2.1.2. Defining Context

In Smith (1994) definition, context is virtually everything that surrounds a stimulus including its relation in space, time, and meaning to the item. Hewitt (1977) separated context into extrinsic and intrinsic context. Extrinsic context is defined as the environment that surrounds the stimulus or stimulus presentation (e.g. being underwater or in a dry classroom during testing), while intrinsic context factors in semantic properties and incidental attributes of the stimulus (e.g. type of font or its color).

This distinction between intrinsic and extrinsic seems to be a bit artificial. Baddeley (1982) pointed out that it is not the type of stimulus that distinguishes intrinsic from extrinsic, but how the participant processes the context. Rather than intrinsic and extrinsic, he suggested a distinction between interactive and independent context. If a context item has a direct influence on how a stimulus is processed during encoding, then it is characterized as interactive. When context item and stimulus are processed and stored separately, they are considered independent. This definition puts the spotlight on the encoding instructions as a determinant of context processing as opposed to the stimulus itself (Gardiner & Tulving, 1980).

A three-dimensional definition of context was proposed by Björk and Richardson-Klavehn (1989) that considers stimulus and context features as well as memory processes such as encoding and retrieval. In their first dimension, they adopted the distinction Geiselman and Björk (1980) recommended: intraitem context (contextual features directly connected to the item) and extraitem context (characteristics not physically connected to the item). In their second dimension, Björk and Richardson-Klavehn suggested that context features may fall into one of three categories: incidental, influential and integral context.

While incidental context does not change the semantic significance of the target-item, influential context has a conscious or unconscious effect on how an item is encoded and integral context is inextricably linked to the stimulus, possibly modifying its meaning. The third dimension describes the influence retrieval processing has on context. Data-driven processing uses perceptual characteristics of the stimulus to retrieve information from memory, whereas conceptual processing employs semantic features.

2.2.1.3. Context Manipulation for Recognition and Recall

Godden and Baddeley (1980) tried to replicate an environmental context effect for recognition in an experiment similar to the diving paradigm (Godden & Baddeley, 1975). The fact that they could not replicate the effect suggested a dissociation of environmental context manipulations between recall and recognition. In a meta-analysis, though, Smith & Vela (2001) did not find sufficient evidence to support that argument. They showed that a reliable context effect can be found in recognition as well as recall memory.

An instinctive notion is that recognition is always superior to recall. If a possible target is made available to participants, one must only match the information provided to the information contained in the memory trace. Tulving and Thompson (1973) provided participants with word-pairs similar to the weak-cue – target pairs in one of their previous experiment (e.g. Train – BLACK; Thompson & Tulving, 1970). Participants were told that they would be tested on the second word. After encoding, they were given a free association task as a supposed distracter (e.g. White – ? "*Provide 4 words that the cue words make you think of*"). Next participants were given a forced choice test, they were suppose to look at their 4 associations and circle the word that was the most likely to have been on the study list. After each pick, they had to indicate their confidence on a scale of 1 to 3, 1 signifying "guess", 2 "reasonably sure", 3 "absolutely sure". In the last part of the test, participants had to recall target words after being presented with the original cue (Train – ___?). Participants supplied 66% of the target words in the free association task, but they only correctly recognized 38% of the generated targets (confidence rating "2" or "3", standard guessing correction applied).

The cued recall test yielded a hit rate of 61%. Consequently, as predicted by the encoding specificity principle, recall can be superior to recognition, when the cue presented at learning is reinstated during cued recall. Here, the semantic context of the target words was changed by providing a novel cue, decreasing memory performance for the target. When the original cue was reinstated, memory performance was superior for cued recall, a test typically considered to be more difficult than recognition. This experiment demonstrates that manipulation of intrinsic or influential context during the retrieval process may vastly influence memory performance.

2.2.2. Recognition Failure of Recallable Words

The recognition failure of recallable words phenomenon, as just described was then studied extensively based on the following paradigm. During encoding, participants are presented with a list of AB-items. They are asked to study the item-pairs so that they can retrieve the B-item (target) with the help of the cue (A-item). In a first retrieval test, where a B-item or a distracter is presented (recognition test), they have to indicate whether or not the item was on the study list. During the second retrieval session they are given the cue item (A-item) and are asked to recall the target (cued recall test).

2.2.2.1. Tulving-Wiseman Function

The relationship between two successive retrieval tests of recognition and recall for a stimulus is described by a function that Tulving and Wiseman (1975) developed. Studying the recognition failure of recallable words paradigm at length, an empirical correlation between recognition and recall was found. It describes the probability of recognition given cued recall as a function of the probability of recognition for all items.

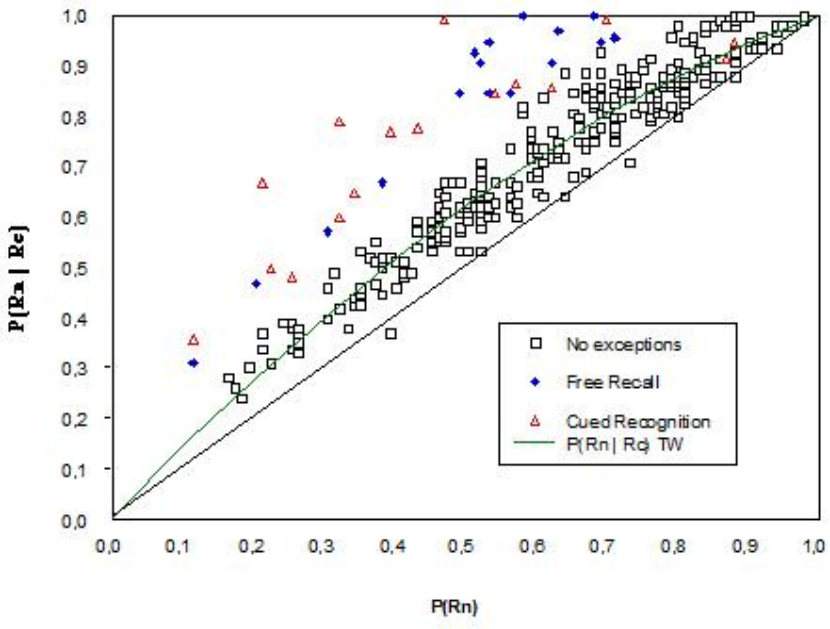

Figure 1: The Tulving-Wiseman Function and its Exceptions (taken from Sikström – The TECO theory and lawful dependency in successive episodic memory tests, 2000): Nilsson and Gardiner's 1993 database. 302 conditions of recognition given cued recall. The dataset is divided into no exceptions, free recall exceptions and cued recognition exceptions. The TW-function is included for comparison.

$$P(Rn|Rc) = P(Rn) + c[P(Rn)-P(Rn)^2]$$

P(Rn|Rc) is the conditional probability for recognition given cued recall, P(Rn) is the probability of recognition and c represents an empirical constant that was approximated to 0.5. This empirical law shows a moderate dependency between recognition and cued recall. In a great number and wide range of studies using the recognition failure of recallable words paradigm and its variations the Tulving-Wiseman functions holds true. In Nilsson and Gardiner's 1993 database, exceptions to the Tulving-Wiseman law were identified on the basis of a greater dependency between recognition and cued recall than the one predicted by the empirical law. The graph in figure 1 illustrates studies from Nilsson and Gardiner's database, including exceptions.

2.2.2.2. Recognition Failure of Recognizable Words – The general contextual account

Gardiner (1994) published a paper that meant to generalize the Tulving-Wiseman function. So far, a moderate dependency is found when a cued recall test is preceded by a recognition test without the contextual cue present. In several experiments Gardiner used a recognition test followed by a cued recognition test and concluded that the conditional probability of recognition given cued recognition also follows the Tulving-Wiseman function. This led him to believe that Tulving-Wiseman function is just an example of a "general contextual account". Gardiner explained that: "This account suggests that such a function might obtain in *any* sequence of successive testing in which the second of the two tests provides different contextual information" (Gardiner, 1994, p. 103).

2.2.3. TECO – A Connectionist Account

An alternative model of memory – the TECO theory – providing an explanation for recognition failure was proposed by Sikström (Sikström 1996b, 2000; Sikström & Lansner, 1995). The term TECO stands for Target, Event, Cue, & Object and is a connectionist model of memory. Sikström proposed this theory to incorporate all data sets of recognition failure into one model to correctly predict the degree of dependence between two successive episodic memory tests. This also includes data sets that do not adhere to the Tulving-Wiseman function and are considered exceptions. To positively predict the measure of dependency between two successive episodic memory tests, it is necessary to find a model that incorporates data about the components and underlying processes that are shared between the two tests. Sikström suggested that: "given certain circumstances the dependency between two tests, measured in a certain way, is approximately proportional to

the proportion of cues shared between the tests" (Sikström, 2000, p. 694, 1996b,). Cues (C), Targets (T), and Events (E) are represented as a distribution of three different node populations (see Figure 2). All nodes are connected to all other nodes as well as within the population (e.g. cue-to-target: C → T, target-to-target: T → T). The nodes may be at either a high or low state of activation and each connection has a certain weight depending on the encoding of a cue-target pair in an event. In this theory, the cue is defined as context to the target word, while the event is the specific time or episode in which the participant encoded the target word. Thus, in one physical contextual setting multiple events can take place (e.g. in a classroom the event "taking a test" or another event "listening to a lecture" are possible).

Another theoretical feature this theory conforms to is the distinction between recollection and familiarity as two separate processes of recognition. While recollection includes the retrieval of specific details from the encoding episode, familiarity signifies successful retrieval of a target in the absence of such encoding details. Recollection is represented as event-to-target connections, while familiarity is described by target-to-target connections.

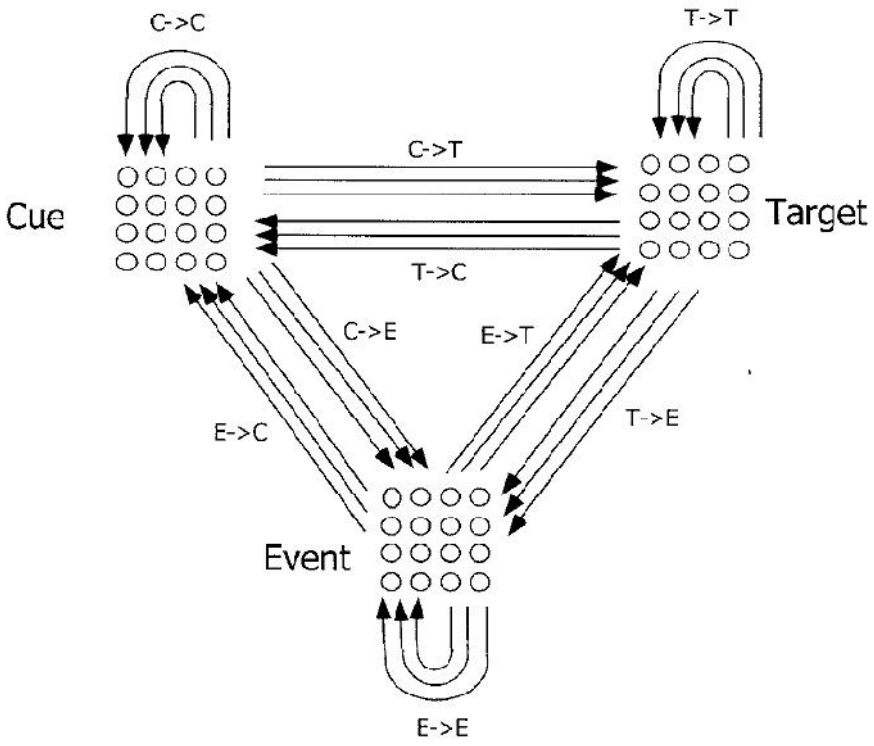

Figure 2: The TECO theory (Sikström, 2000): The circles symbolize the nodes in the cue (C), the target (T) and the event (E) populations. The arrows indicate the connections between the populations, e.g., E → T are the connections from the event population to the target population.

Sikström and Lansner (1995) applied the TECO theory in a connectionist network and mathematically solved the problem in what they called the explicit solution. It describes the conditional probability of the correct activation in one node. A disadvantage of the explicit solution was found to be the limit in practicability when trying to find the proportion of shared components in the network between the two tests. This constraint was overcome by a proposal of Sikström (1996b, 2000) to introduce a dependency measurement β_t. This measurement is the predicted (t = theoretical) degree of dependency between two successive tests. The term β_t is calculated by dividing the number of shared connections with the number of all connections of two successive tests. If no connections are shared between two successive tests, they are considered independent of each other ($\beta_t = 0$). If all connections are shared, the tests are identical ($\beta_t = 1$). From these definitions one may calculate the theoretical dependency β_t for recognition followed by cued recall. The connection event-to-target (E → T) is shared by both tests. Three connections are formed in this paradigm: target-to-target (T → T), cue-to-target (C → T), and event-to-target (E → T).

Recognition	T → T; E → T;
cued recognition	T → T; C → T; E → T
free recall	E → T
cued recall	C → T; E → T

The theoretical dependency between these two test is therefore 1/3 ($\beta_t = 1/3$).

From this theoretical measurement of dependence Sikström developed a function to predict the conditional probability of recognition given recall (or an un-cued retrieval test followed by a cued retrieval test). Note that the explicit solution of the connectionist network has no mathematical connection to this function. Sikström (2000, p. 700) rather described the relationship between the two functions: “two different ways of approaching the same underlying idea.”

2.2.4. Recognition – Recollection and Familiarity

The Tulving-Wiseman law considers recognition memory to be a unitary phenomenon. Some evidence has been discovered that points towards two dissociable components of recognition memory based on different states of awareness (e.g. Gardiner, 1988; Jacoby, 1991). While recollection requires the participant to retrieve qualitative information about the encoding episode (e.g. where and when the target was presented), familiarity is based on judgment of memory strength without retrieval of a contextual detail. An example is experience of recognizing a familiar face but not being able to remember who

the person is or where and when the person was encountered before (e.g. Tulving, 1983, 1985a, 1985b, 1989; Sikström & Gardiner, 1997; Yonelinas, 2002; Diana et al., 2007). A famous illustration of this experience by George Mandler is the butcher-on-the-bus phenomenon. Imagine taking the bus and seeing a familiar face among the riders, without being able to place the person. The identity of the individual remains unclear due to the changed setting of the bus. Later on, the person is encountered in his apron in the butcher shop and immediately recognized as the butcher himself (Mandler, 1980; Yovel & Paller, 2003).

Properties of recollection compared to familiarity are extensively examined by Yonelinas (2002). Most theories advocate a parallel initiation of both processes for any retrieval attempt, with familiarity believed to be faster than recollection. While recollection signifies successful retrieval of contextual encoding details, familiarity is a function of memory strength. Familiarity also seems to be a relative automatic process compared to the increased cognitive control processing necessary to complete recollection. Yonelinas (2002) also concludes that familiarity should support encoding of new items, but does not sustain learning of associations between item pairs.

Recollection and familiarity show a differential dependency between recognition and cued recall. While recollection reveals a significantly larger dependency between recognition given cued recall, familiarity responses show a smaller dependency on recognition failure than the Tulving-Wiseman function predicts (Sikström & Gardiner, 1997). Further evidence for possible interdependency between familiarity and recollection processes will be examined later on.

2.3. Neural Representation of Episodic Memory

2.3.1. Imaging Contextual Memory – A Critical Difference in Approach

2.3.1.1. Imaging Recollection and Familiarity

Several approaches to extract the neural correlates of recollection and familiarity are commonly used in recognition studies. In the remember/know procedure participants are asked during retrieval to judge whether an item is recognized due to the retrieval of a specific contextual detail about the encoding episode or independent of contextual information (e.g. Uncapher & Rugg, 2005; Fenker et al., 2005; Slotnick, 2010). In a remember/know paradigm participants are not asked to specify what contextual detail led to the remember judgment. Consequently, it remains unclear to the experimenter what exact criterion participants use to judge the presence of a contextual detail and how confident they are about recognizing an

item. In an effort to address some of these problems confidence ratings were introduced into experimental paradigms. Participants are asked to categorize an item as remembered when they recalled a specific detail about the encoding episode and in absence of such detail rate their confidence in positively recognizing the target (e.g. Yonelinas et al., 2005; Montaldi et al., 2006).

Nevertheless, using the remember/know paradigm experimenters are unable to establish what exact detail the participant used to determine recollection. A different approach to image recollection is the source memory paradigm. Participants are asked to place a stimulus in a specific context of the encoding episode, for example, color of the item, position on the screen, affiliation to a certain study list. Neural correlates of recollection and familiarity are calculated by differences in source and item memory (e.g. Ross & Slotnick 2008; Gold et al., 2006). While source memory is believed to be either present or absent, familiarity may not be quite as uniform, but rather a continuum of recognition confidence. Recognition confidence ratings for item memory are used to refine source memory paradigms (Ranganath et al., 2003).

In a more complex experimental set-up participants may be asked to remember a specific inter-item association instead of a single stimulus. Recollection in these paradigms is identified with associative memory, while non-associative memory is thought to be connected with familiarity. During encoding, participants studied, for example, a list of word-pairs, a combination of objects or an object paired with verbal material (A-B). At test, participants are asked to indicate whether or not the presented stimuli were part of the study list, and crucially, whether or not the association between the stimuli (e.g. face-name, word-pair) was intact (A-B or A-C). Recognition of presented pairings indicates associative memory and thus recollection, while non-associative memory for an item indicates familiarity (e.g. Kirwan & Stark, 2004).

In all of the above tasks, participants are asked directly about the contextual setting of the stimuli during the retrieval task. This encourages participants to consciously encode the context into and specifically retrieve it from memory.

2.3.1.2. Incidental Contextual Memory

Tulving and Gardiner's unique approach to investigating context in episodic memory was to be indirect, leaving the participant unaware of the manipulation. Environmental context manipulation akin to in Godden & Baddeley's scuba-diving experiments or a simple change of rooms in between encoding and retrieval treat context as a seemingly incidental covariant to the participant. For the semantic context manipulation used in this study the same may be assumed. Participants are not directly asked to remember the context provided during study, but are asked to judge whether a target-item has been presented previously

independent of its context. Although the term incidental context was defined by Björk & Richardson-Klavehn (1989) as a contextual influence that does not influence the semantic processing of the target-item, here, an influence of the accompanying semantic context on the target-item is assumed to be in effect to facilitate the behavioral effect. The term incidental is used to describe the indirect approach to context manipulation as compared to paradigms using a direct line of questioning with participants to determine the presence of contextual information in memory.

2.3.2. The Medial Temporal Lobe and Episodic Memory

2.3.2.1. Anatomy of the Medial Temporal Lobe

The medial temporal lobe is an area of the brain that includes the hippocampus, the perirhinal cortex (PRC), the parahippocampal cortex (PHC), and the entorhinal cortex. The parahippocampal gyrus encompasses the parahippocampal cortex in the posterior and the perirhinal cortex in anterior part of the gyrus. The parahippocampal gyrus in addition to the entorhinal cortex is also referred to as the parahippocampal region. The hippocampus proper includes the dentate gyrus, fields CA3, CA2, and CA1, while the hippocampus formation also includes the subiculum (Witter et al., 2000; Dickerson & Eichenbaum, 2010).

The entorhinal cortex may be functionally differentiated in a medial and lateral area (Kerr et al., 2007), also anatomical evidence for this distinction is only available for nonhuman primates and rats. When referring to the human medial temporal lobe, the anterior parahippocampal gyrus is regarded to include the perirhinal cortex and the lateral entorhinal area, while the posterior parahippocamal gyrus is thought of in terms of including the parahippocampal cortex and possibly the medial entorhinal cortex (Burwell, 2000; Eichenbaum et al., 2007).

2.3.2.2. Functional Organization of the Medial Temporal Lobe Supporting Memory Processes

Anatomical studies suggest that inputs to the medial temporal lobe arrive via neocortical association areas. Unimodal visual and semantic information, also called the "what"-stream, enter primarily through the perirhinal cortex, while primarily polymodal visual-spatial information but also unimodal inputs ("where"-stream) connect to the parahippocamal cortex.

In the so-called "what"-stream, unimodal information about objects, targets, and their characteristics is encoded (Suzuki & Eichenbaum, 2000; Eichenbaum, 2006). The "where"-stream includes temporal and especially spatial information of the encoding event and its

contextual setting (Hargreaves et al., 2005; Suzuki & Amaral, 2004; Eichenbaum & Lipton, 2008).

Although connections between the perirhinal and parahippocampal cortices exist, the two streams remain functionally separate from each other. They also do not converge in their shared main projection area the entorhinal cortex, but are separately processed: perirhinal input in the lateral entorhinal cortex and parahippocampal gyrus input in the medial entorhinal cortex (Witter et al., 2000; Kerr et al., 2007; Suzuki & Amaral, 2004). The primary projection of the entorhinal cortex is the hippocampus (Kerr et al., 2007). The hippocampus may be divided into four subdivisions that process input in a unidirectional pathway starting from dentate gyrus passing through CA 3, to CA 1 and finally ending in subiculum (Dickerson & Eichenbaum, 2010). Not until the "what" and "where"-streams reach this area of the medial temporal lobe are they jointly processed. But not all of the four subdivision of the hippocampus integrate the incoming projections. While the dentate gyrus, CA 2, and CA 3 integrate the streams, in CA 1 and subiculum they remain separate (Bakker et al., 2008; Dickerson & Eichenbaum, 2010). Dickerson & Eichenbaum (2010, p. 5) suggest that by this measure, the hippocampus may "associate and distinguish events and the context in which they appear" (also see Witter et al. 2000, Bakker et al., 2008). Outputs from the hippocampus inversely retrace the steps of input information (Eichenbaum, 2006; Eichenbaum & Lipton, 2008, Dickerson & Eichenbaum, 2010).

2.3.2.3. Medial Temporal Lobe Amnesia

Patient and animal lesion studies indicate that damage to the hippocampus and adjacent parahippocampal region cause amnesia. The amnesic syndrome may stem from various neurological etiologies, e.g., Korsakoff syndrome, encephalitis, vascular disease, Alzheimer's disease, or tumors. In the case of one of the most famous amnesic patients H.M. though, it resulted from a bilateral medial temporal lobe resection (Scoville & Milner, 1957). This operation was performed in 1953 after the source of H.M.'s poorly manageable epilepsy was located in the right and left medial temporal lobes. The surgery destroyed approximately two-thirds of the anterior hippocampus and the hippocampal gyrus (Scoville & Milner, 1957), including parts of the parahippocampal gyrus, all of the entorhinal cortex, and the amygdala. The ventrocaudal perirhinal cortex and the posterior parahippocampal cortex remained largely intact (Corkin et al., 1997; Corkin, 2002). After waking up from the surgery, H.M. had not only lost the physical source of his epileptic disorder, but also the main source of his brain responsible for the formation of new memories. From that moment on, H.M. suffered from retrograde amnesia, primarily of the 11 years before the surgery (Sagar et al., 1985; Corkin, 2002) and anterograde amnesia. The anterograde amnesia prevented him to commit new events as well as new semantic knowledge (Gabrieli et al., 1988) into long-term

declarative memory. Working memory and procedural memory (Corkin, 1968) remained intact. Despite these limitations, H.M. showed normal intellectual abilities and language skills (lexical and grammatical processing) for a man of his education and socioeconomic background (Kensinger et al., 2001; Milner, Corkin, & Teubner, 1968). Although, H.M. showed severe impairment of spatial memory, he was still able to draw a detailed map of the house he and his parents had moved into after the surgery. Milner et al. (1968) also noticed that when asked for directions home, H.M. indicated the way to the street where he used to live with his parents before the operation, though he did know upon arrival that this was not the correct address. When they arrived in the vicinity of his new home, "he seemed to be familiar with the topography of the immediate neighborhood," (p. 217). Corkin (2002, p. 156) explained this remarkable exception to his condition as follows: "H.M. acquired the representation after the onset of his amnesia. Presumably, he was able to construct a cognitive map of the spatial layout of the house as the result of daily locomotion from room to room, thereby encoding the location of each room in relation to the other rooms." Many of the anatomical correlates for topographical memory were still intact in H.M. brain, especially the caudal part of the right parahippocampal gyrus (Corkin, 2002; Corkin et al., 1997). Lesion studies have shown that this area might be a strong neural correlate for spatial memory (Bohbot et al., 1998).

A strikingly similar patient was first studied by Moscovitch in 1983. Patient K.C. suffered brain damage from a traumatic head injury following a motorcycle accident at the age of 30 in 1981. After his release from a rehabilitation hospital, it became apparent that he was severely restricted at committing new information into memory. For episodic memory in particular, he showed severe anterograde and retrograde amnesia, while semantic knowledge of personal and general facts accumulated before the accident remained intact. Any details his mind might have stored about his personal life and the events that occurred in the last 30 years before the accident are either lost or inaccessible to him. While he is unable to form any new personal memory about his daily life, K.C. is still able to learn new factual information and concepts (for a review see Rosenbaum et al., 2004).

2.3.3. Theories of Episodic Memory

2.3.3.1. Models of Neural Representation of Episodic Memory in the Medial Temporal Lobe

Two theories of the neural representation of episodic memory are prominent in current memory research. Both theories offer an approach to the neural representation of the widely accepted theoretical and behavioral distinction of recognition memory into recollection and familiarity. While the single process models propose that recognition is a quantitative

continuum on an axis between the feeling of remembering and the feeling of knowing supported by the same neuronal system, the dual process model assumes that recognition memory for recollection and familiarity is supported by two distinct neuronal processes. Among dual-process supporters, recollection is generally assumed to be dependent on the hippocampus, while familiarity is believed to rely on perirhinal cortex activity.

2.3.3.2. The Single-process Model of Recognition Memory: Signal-detection Theory

Studies of recognition memory suggest that recollection may depend on the hippocampus, while familiarity is created by perirhinal cortex operations. Assuming recall is dependent on recollection, while recognition may be accomplished by either recollection or familiarity (Mandler, 1980), isolated lesions of the hippocampal cortex affecting recall should spare recognition. Evidence from group studies of bilateral hippocampal lesion patients indicates the opposite, arguing that previous associations of hippocampal damage to a preferential impairment of recall compared to recognition are based on studies of individual participants (Squire, Wixted, & Clark, 2007). After careful analysis of the available data Squire et al. (2007) found similar impairment for recognition and recall among amnesiac patients (Wixted & Squire, 2004; Manns et al., 2003; Kopelman et al., 2007). The signal-detection theory proposes that paradigms of remember/know judgments and confidence ratings without source recollection measure recognition memory in terms of memory strength in relation to a response criterion (Wixted, 2007). Independent of behavioral measures of recollection or familiarity, strong memories may yield increased hippocampal activity. No association with hippocampal activity is found for weak memories, which reflect no absolute delimitation between weak familiarity, weak recollection, or both. Thus, both recollection and familiarity seem to depend on hippocampus and perirhinal cortex (Squire, Wixted, & Clark, 2007; Wixted, 2007).

2.3.3.3. The Dual-process Model of Recognition Memory: Recollection and Familiarity

Advocates of dual-process theories cite studies of amnesiac patients suffering from focal brain lesions who show memory deficit for recollection that leaves familiarity intact (refer to Eichenbaum et al., 2007 for review). A separate neuroanatomical medial temporal lobe basis for the two qualitative processes relaying recollection and familiarity are first proposed by Eichenbaum and colleges (1994). They suggest that the parahippocampal region supports item-memory, while the hippocampus processes relationships among items as well as specific memories for events. Eldridge et al. (2000) reported hippocampal activity only for retrieval of consciously recollected details. In their remember/know paradigm, “know” answers indicating familiarity yielded no increased hippocampal activity compared to misses or correct rejections. In a review considering animal models of neuronal recordings, animal

and clinical lesion studies, and human imaging studies Brown and Aggleton (2001) concluded that recollection dependents on the hippocampus, while familiarity is represented by perirhinal cortex activity.

2.3.3.4. The BIC Model

Expanding on the dual process model, Eichenbaum et al. (2007) proposed a three-component model for recollection and familiarity. Individual regions of the medial temporal lobe are assigned specific sub-functions of recognition based on behavioral, neuropsychological, and neuroimaging studies (Eichenbaum, Yonelinas, & Ranganath, 2007; Diana, Yonelinas, & Ranganath, 2007). Like several different theories before, a central role was allotted to the perirhinal cortex for the support of familiarity-based recognition at encoding and retrieval (Fernandes & Tendolkar, 2006; Weis. et al., 2004). Two regions that support different aspects of recollection were suggested as a neuroanatomical correlate for recollection. The parahippocampal cortex is essential to recollection by encoding and retrieving spatial and non-spatial contextual information, while the hippocampus supports the "binding of item and context" (BIC) during encoding (Diana, Yonelinas, & Ranganath, 2007).

The neuronal activation pattern of the MTL to a stimulus is subject to what type of processing is used and the cues presented during encoding and recognition. During encoding of items that are later judged familiar, the perirhinal cortex will show increased activity. Throughout cued retrieval of these items, the perirhinal cortex will be deactivated. This deactivation will then lead to judgment of familiarity. Additional input to the hippocampus might point to the activation pattern at encoding and lead to re-instatement of the events by reactivating the contextual information in the parahippocampal cortex network. If the input was strong enough to allow pattern completion in the hippocampus, an item will be recalled in its contextual setting and a recollection-based judgment is made. A similar pattern should be observed when presenting a studied context. If the context is reinstated at test, deactivation is observed in the parahippocampal cortex, leading to input to the hippocampus with should allow association of an item to the context. Recollection-based item recognition is then achieved by activating the perirhinal cortex.

The model predicts that deactivations in the perirhinal and parahippocampal cortices will occur in a cued (item or context) recognition test, while activation will occur for un-cued retrieval of items or contexts. Consequently, the pattern of activation in the MTL depends on the test parameters at encoding and retrieval.

2.3.4. Neural Correlates of Episodic Encoding outside Medial Temporal Lobe

2.3.4.1. The Subsequent Memory Effect

To correlate successful long-term memory encoding, a method called the subsequent memory effect was first used for analyzing event-related potentials (Sanquist et al., 1980) and later in PET and fMRI studies (for a review see Wagner et al., 1999). Event-related activity during an encoding task is contrasted by the results from a subsequent memory test according to remembered and forgotten items. This effect is sometimes also referred to as the Dm effect: Differential neural activity based on memory (Paller et al., 1987).

2.3.4.2. The Role of the Prefrontal Cortex in Episodic Memory Encoding

In studies employing the subsequent memory paradigm, the inferior prefrontal cortex (PFC) has long been associated with successful episodic encoding (Rugg, Otten, & Henson, 2002; Blumenfeld & Ranganath, 2007). Frontal encoding activity is associated with strategic organization of study material, including items and context (Davidson et al., 2006). While the left PFC seems to be active preferentially during processing of verbal encoding material (Otten & Rugg, 2001b; Wagner et al., 1998b; Paller & Wagner, 2002), the right PFC was reported active for visual stimuli (Brewer et al., 1998). Sub-regions of PFC appear to be responsible for different aspects of the encoding process. The subtask of the ventrolateral prefrontal cortex (VLPFC) located in and around BA 44, 45, and 47 seems to be in selecting the relevant item information in working memory from a great stream of input arriving from the sensory systems. The VLPFC draws attention to the relevant information or inhibits irrelevant information (Blumenfeld & Ranganath, 2006). The selection and maintenance of semantic information seems to be realized predominantly in the anterior and ventral regions of the VLPFC (BA 47, 45), while the posterior and dorsal VLPFC (BA 44) processes semantic, phonological, or orthographical word characteristics (Poldrack et al., 1999; Gold & Buckner, 2002; Blumenfeld & Ranganath, 2006, 2007). In general, strong evidence points toward the involvement of VLPFC in successful episodic encoding. Murray and Ranganath (2007) specified its role in long-term memory formation by showing that VLPFC activation predicts successful memory for items and associations.

Another sub-region of the PFC, the dorsolateral prefrontal cortex (DLPFC) including BA 46 and 9, has presented researchers with a less clear-cut pattern of activity. Compared to ventrolateral part of the prefrontal cortex, the dorsolateral region is rarely linked to successful long-term memory formation. Studies using the subsequent memory effect were summarized by Blumenfeld and Ranganath (2007). While 132 out of 150 local maxima in the PFC are located inside VLPFC, only 18 are found within the DLPFC. The DLPFC not only shows a

weak relationship to successful encoding, but a reverse relationship between subsequent memory and the DLPFC seem to be implied by some study results. A correlation between subsequent forgetting and the activation in the DLPFC was found (e.g. Otten & Rugg, 2001a; Wagner et al., 1998b; Blumenfeld & Ranganath, 2006). Looking at the role of DLPFC in cognitive control might be helpful to clear up the picture. Neuroimaging studies have suggested a role of the DLPFC in organization of items active in working memory (Postle et al., 1999; D'Esposito et al., 1999; Ranganath & D'Esposito, 2005). The term organization of working memory may refer to any of the following processes: comparing two items present in working memory to each other, changing their relationship amongst each other, e.g. change of sequence or chunking, which entails reorganization of items into units (for a review see Blumenfeld & Ranganath, 2007). This process of organization or manipulation may lead to increased inter-item association and thus promote long-term memory formation (Bower, 1970). The inability to positively associate long-term memory formation and activity in the DLPFC may therefore be explained by a lack of an appropriate encoding task to recruit the presence of DLPFC activation in a subsequent memory effect. If organization and the formation of a new relationship amongst study items present in working memory are not required, the encoding capability of the DLPFC remains idle (Blumenfeld & Ranganath, 2006, 2007). The DLPFC is therefore preferentially activated during relational encoding and predicts successful memory for associations (Murray & Ranganath, 2007).

2.3.5. Neural Correlates of Episodic Retrieval outside Medial Temporal Lobe

2.3.5.1. The Retrieval Success Effect

An experimental paradigm that scans participants during retrieval of previously studied items may lead to the detection of retrieval activity. Retrieval events are contrasted by successfully retrieved targets versus correctly rejected distracters (i.e., hits > CR). By contrasting successful retrieval versus successful rejection, only items with a reliable memory trace are included in the analysis (Buckner et al., 1998; Spaniol et al., 2009). This effect is also called the "old-new effect" (Henson, 2005).

2.3.5.2. The Frontal Cortex and Episodic Retrieval

Frontal cortex activity is almost universally found in episodic retrieval paradigms. In terms of the magnitude of measured activity it shows by far the strongest activation pattern at encoding, but seems to run second to parietal activity at retrieval. Spaniol et al. (2009) cite mainly left-lateralized ventrolateral and dorsolateral prefrontal cortex activity (VLPFC, DLPFC), right and left lateral anterior prefrontal cortex (anterior PFC), and left anterior

cingulate activity for retrieval success. Activity in the inferior frontal gyrus is present in retrieval success studies, but secondary to frontal activity in the middle and superior frontal gyri.

Retrieval is a complex process requiring several cognitive operations to complete the task. While retrieval itself is accomplished by structures of the medial temporal lobe, pre-and post-retrieval processing requires frontal cortex assistance. Before attempting to retrieve information, cognitive control processes need to engage retrieval mode, an operation necessary to start a retrieval attempt. The right anterior prefrontal cortex (aPFC; BA 10) is associated with retrieval mode, which is a sustained control process across trials (Velanova et al., 2003). Retrieval orientation depends on the retrieval cues presented, and retrieval effort is exerted according to task difficulty. Simons, Gilbert et al. (2005) propose that the lateral aPFC (BA 10) and ventrolateral prefrontal cortex (VLPFC; BA 47) is involved in control operation necessary for the specification of the retrieval process, e.g. orientation on the retrieval cue, regardless of the occurrence of an actual retrieval search. A similar claim is made by Dobbins et al. (2002) who attribute monitoring and evaluation of the retrieval cue to the left aPFC and posterior DLPFC and controlled retrieval of semantic information to the left anterior VLPFC (Dobbins et al., 2002; Dobbins & Wagner, 2005). The anterior VLPFC specifies the cue during the retrieval attempt. In a second paper of 2005, Simons, Owen et al. suggested a role in general processing of contextual information of the lateral aPFC. It must be noted that all of these studies put the role of the aPFC and VLPFC into a pre-retrieval time frame; these areas activate independent of later retrieval success or failure.

If a conclusive retrieval operation is not accomplished by automated matching of target and retrieval cue (Buckner, 2003), post-retrieval processing becomes necessary to reach the task goal. The desired information is maintained and selected among competing irrelevant information before a retrieval decision may be reached. While control of recollective monitoring is exercised by the posterior dorsolateral prefrontal cortex (DLPFC) and aPFC, Dobbins et al. (2002) assign phonological maintenance and rehearsal to the posterior VLPFC. As for selection, Buckner (2003) elaborates on a dissociation of the VLPFC substructures depending on cognitive control. The amount of control required to perform a certain selection task determines which part of the VLPFC is recruited. If a cue leads to direct retrieval of information, thus requiring less selection control, only the posterior part of the VLPFC is recruited. For greater selection control, anterior regions of the VLPFC (BA 44/45/47) are additionally activated (Buckner, 2003; Gold & Buckner, 2002). The region between anterior and posterior VLPFC, the left mid-VLPFC (BA 45/44) is also associated with selection of retrieved information by Badre et al. (2005), resolving inference between competing retrieved information. The left anterior VLPFC (BA 47), conversely, implements top-down controlled retrieval of semantic knowledge. If the desired information is not

retrieved automatically, the left anterior VLPFC may actively access “long-term semantic representation stored in lateral temporal regions” (Badre et al., 2005, p. 915). Another frontal cortex region, the right DLPFC, is often associated with post-retrieval monitoring (Henson et al., 2000; Fletcher & Henson, 2001). Fleck et al. (2006) found that this activity is not specific to post-retrieval monitoring in episodic retrieval, but suggests a broader role in general decision-making shared by memory and non-memory tasks (visual perception). Along with studies of working memory and attention, Fleck proposes a role in evaluation of accumulated information and response selection for the right DLPFC rather than post-retrieval maintenance.

2.3.5.3. The Parietal Cortex and Episodic Retrieval

For a general impression on the involvement of the parietal cortex in episodic retrieval studies refer to Spaniol et al. (2009). The meta-analysis of 30 retrieval studies that use old-new recognition judgments to investigate retrieval success concludes that the parietal lobe in general shows a stronger association to retrieval success than encoding success. The inferior lateral parietal lobe activity is even almost exclusively associated with retrieval success.

Wagner et al. (2005) performed a multi-study analysis for parietal lobe activity in retrieval success studies. An old/new effect (hit versus correct rejection) activity was found in precuneus, posterior cingulate, retrosplenial cortices, and left lateral parietal cortex (including intraparietal sulcus, inferior parietal lobule, superior parietal lobule) in all contrasts. An increase in parietal activity is also found for retrieval success compared to retrieval failure (hit versus miss). Neuroimaging studies have pinpointed specific characteristics of parietal lobe function for episodic retrieval. Activity in certain parietal regions is associated with recollection, in others with familiarity (Daselaar, Fleck & Cabeza, 2006; Yonelinas, Otten, Shaw & Rugg, 2005). Perceived oldness independent of the true nature of the item is linked to parietal cortex activity in the left parietal cortex (BA 40, 39; Wheeler & Buckner, 2003). Additional imaging results connect an attempt to retrieve source information, as opposed to item information, independent of response accuracy, to specific parietal areas (Dobbins et al., 2002).

In an effort to integrate all features of parietal activity into one working hypothesis, two parallel theories used essential aspects of attention theory (Corbetta & Shulman, 2002) on memory retrieval. Both were published online simultaneously in 2008 and describe similar patterns for the parietal cortex in memory retrieval. The first reviewed for the purposes of this thesis is the dual attention processes hypothesis (DAP) by Cabeza (2008) which will be described in a short summery followed by the attention to memory hypothesis (AtoM) by Ciaramelli et al. (2008).

2.3.5.4. The Dual Attention Processes Hypothesis

Applying episodic memory retrieval processes to the parietal cortex, Cabeza (2008) differentiates between two specific areas of the parietal cortex: The dorsal parietal cortex (DPC) located in the lateral parietal region around the intraparietal sulcus (BA 7) and the ventral parietal cortex (VPC) situated in the supramarginal and angular gyri (BA 40, 39). In their attention research, Corbetta & Shulman (2002) describe a dorsal fronto-parietal system (DPC) that supports top-down attention processes, while bottom-up attention is maintained by a ventral-parietal system (VPC). While top-down attentional processes are goal-driven and intentional, bottom-up processes are associated with cue saliency and task relevance of to be processed stimuli (Vilberg & Rugg, 2008). Incoming information may stem from environmental input or memory (Cabeza, 2008).

In the dual attentional processes hypothesis, Cabeza proposes episodic memory components that may direct attention from the top-down as well as the bottom-up perspective. Top-down attention occurs when an attempt is made to retrieve specific information from memory. Memory driven bottom-up attention occurs when a coincidental input leads to unintentional remembering or when a conscious search for a specific memory culminates in an unsuspected retrieval outcome. Cabeza (2008) used the example of "remembering if you paid the electric bill, you may recall the wedding invitation that was next to the bill in your mailbox," p. 1815). The goal to remember is initiated in the frontal cortex and driven by the DPC. Top-down attentional processes maintain retrieval for a specific target from memory through the medial temporal lobe, while retrieval output is monitored for its relevance to the task by bottom-up attentional processes in the VCP. Retrieval output processed in the VCP may then alter the original goal maintained in the DCP (Cabeza, 2008).

2.3.5.5. The Attention to Memory Hypothesis

A model somewhat similar in certain aspects of functional differentiation is proposed by Ciaramelli, Grady & Moscovitch (2008), called the attention to memory hypothesis (AtoM). Specific parietal activities and their function for episodic memory retrieval are based on attention theory. The two attentional systems in the parietal lobe (Corbetta & Shulman, 2002) play different roles in memory retrieval. The superior attentional system, including the superior parietal lobe and the intraparietal sulcus (BA 7, 19), supports top-down attention to memory, while the inferior attentional system, represented by the inferior parietal lobe and the temporoparietal junction (BA 40, 39), is associated with bottom-up attention to memory. A distinction between two retrieval modes is made; direct retrieval occurs when the presented cue interacts directly with the memory system located in the medial temporal lobe, whereas indirect memory occurs if the cue does not automatically lead to the target memory. If the

stimulus is unable to trigger target memory autonomously, additional "strategic retrieval processes" are necessary. These additional processes include further retrieval attempts and post-retrieval monitoring, accomplished by frontal cortex areas but initiated by the superior parietal lobe (BA 7, 19).

Bottom-up capture of attention by memory is perceived when the cue directly triggers stored information in the medial temporal lobe. No additional retrieval attempts or monitoring operations are necessary to identify the correct pathway leading to the target information. The inferior parietal cortex, thus "mediates automatic, bottom-up attentional capture by the recollected memory contents" (Ciaramelli et al. 2008 p. 1828). Ciaramelli et al. (2008) further suggest that the inferior parietal lobe activity is necessary to transfer the memory into consciousness. The same proposal is made by Vilberg and Rugg (2008, p. 1794), who claim that the "inferior parietal cortex acts as an interface between episodic memory and the executive systems [prefrontal cortex areas] that monitor and control on-line processing." The inferior parietal cortex thus aids the conscious representation of directly retrieved episodic memories by its function in capturing bottom-up attention to memory. This theoretical detail connecting attention to memory would relate well with studies of patients suffering from parietal lesions and symptoms of neglect. Despite the fact that all sensory areas of the brain are working properly and the person is conscious, patients with parietal lesions are not able to see, feel or hear any stimulus on the contralateral side of the damaged brain region or even consciously experience the equivalent body half. With intense physical therapy, they gradually regain some functions of the disregarded body side, by consciously focusing attention from the healthy half of the body to the diseased area. For memory studies on patients with parietal lesions and neglect refer to Davidson et al. (2008) and Ciaramelli et al. (2008).

2.3.5.6. Implications for the Current Study

When investigating the recognition failure of recognizable words phenomenon, it is necessary to differentiate between context-dependent forgetting and context-independent forgetting. The present study outlines this distinction by using two successive recognition tests. During the first recognition test a different context condition to the encoding episode was used for cued recognition, at the second recognition test the original context conditions were reinstated during cued recognition. This set-up did not only provide information about context-dependent memory, but also allowed insight into cue-dependent retrieval processes. It was hypothesized that in a same context condition, direct retrieval of the encoded item should have been accomplished by bottom-up attention to memory anchored by the inferior parietal lobe and temporoparietal junction; furthermore, in a different context condition top-

down attention to memory – supported by areas in the superior parietal lobe and intraparietal sulcus – was necessary to facilitate retrieval of the correct information indirectly.

2.4. Neural Correlates of Context-dependent Memory

Although the recognition failure of recognizable words phenomenon has been exhaustively studied in terms of the behavioral effect, a direct translation into functional magnetic resonance imaging has never been tried in this manner before. Based on Gardiner's behavioral work (1994), the present study adjusted the paradigm for fMRI to explore the neural correlates of context-dependency. At encoding, participants were presented with word-pairs consisting of a target-item and a semantic context-item. Encoding was followed by two consecutive recognition tests. In both recognition tests, the target-item was presented with a semantic context-item, but in the first recognition test the original context-item was replaced by a strongly associated but novel context-item (different context condition), while the original context-item was reinstated in the second recognition test (same context condition).

Encoding activity was investigated based on later retrieval success or failure in the presence or absence of the original context cue. The subsequent memory paradigm may reveal encoding activity that facilitates later occurrence of context-dependent retrieval. Scanning during the first recognition test, in which the semantic context is changed, should identify the neural correlates of the processes involved in context-dependent forgetting. Similarly, in the final stage of the experiment in which the encoding semantic context is reinstated, the neural correlates of context-dependent remembering may be investigated. Areas of interest hypothesized to be in a causal relationship with the event of recognition failure of recognizable words for episodic encoding and retrieval are expected to be located mainly in the medial temporal lobe. According to the BIC model, the hippocampus and the parahippocampal cortex, in particular, are associated with context-memory as compared to item-memory (Diana et al., 2007).

3. Material and Method

3.1. Participants

Twenty-four healthy, right-handed, adult volunteers took part in the experiment. Participants were recruited from the database of the Center for Advanced Imaging (Department of Neurology, Otto-von-Guericke University of Magdeburg, Germany). Four participants were replaced for a low number of items showing the behavioral effect and three participants were later removed from the analysis due to a misbalance among item categories. While showing the behavioral effect, they yielded an insufficient number of items forgotten throughout the experiment. After replacing and removing participants from the analysis, a total of 21 participants remained – thirteen men and eight women (mean age 25.2, R = 20-33, SD = 3.02). German is the first language of all participants. Informed consent was obtained prior to the experiment. All participants had previous experience in the scanner and were later paid for their participation.

3.2. Test

3.2.1. Stimuli

300 word-triplets were used from the University of South Florida Free Association Norms (Nelson, McEvoy, & Schreiber, 1998), translated into German and adjusted to account for linguistic and cultural differences (refer to appendix C for a list). The target word of the group (B) was selected to be weakly associated with one of the words in the group (A) and strongly associated with the other (C), (e.g. target: “SCHNEEMANN”; weak: “schmelzen”; strong: “winter”). The 300 triplets were divided into three blocks of 100 word-triplet. For each participant the words were randomized in their order of presentation and arbitrarily selected as target word-triplets (80/100) or distracters-triplets (20/100). The target and weak semantic context word were presented together during encoding (AB). The weak context word was replaced by a strong context word, meaning closely associated word, in the first recognition test (CB). In the subsequent second recognition test, the original, weakly associated context word and target were again used as cue for retrieval (AB). The presentation order of the blocks was counterbalanced for testing. Stimuli were always presented in pairs in the middle of the screen.

3.2.2. Procedure

Participants were given oral instructions aided by an instruction booklet (see appendix A and appendix B). After these instructions, a short demonstrative version of the first task was presented on a computer, where participants were given the opportunity to practice to be able to adjust to button combinations and speed. This was necessary to achieve close to optimal performance in the scanner from the beginning. Neither the filler task, nor the subsequent recognition tests were practiced before testing in the scanner started.

3.2.3. Testing Parameters - Paradigm

The test was divided into three completely separate but identically constructed blocks with four sessions per block – the encoding session of a semantic word-pair followed by a distracter task and two cued recognition tasks. In the first recognition task, participants were presented with a cue that consists of the encoded target and a novel closely associated contextual semantic stimulus to the encoded target. During the second recognition task, the presented cue included the target and the originally encoded context.

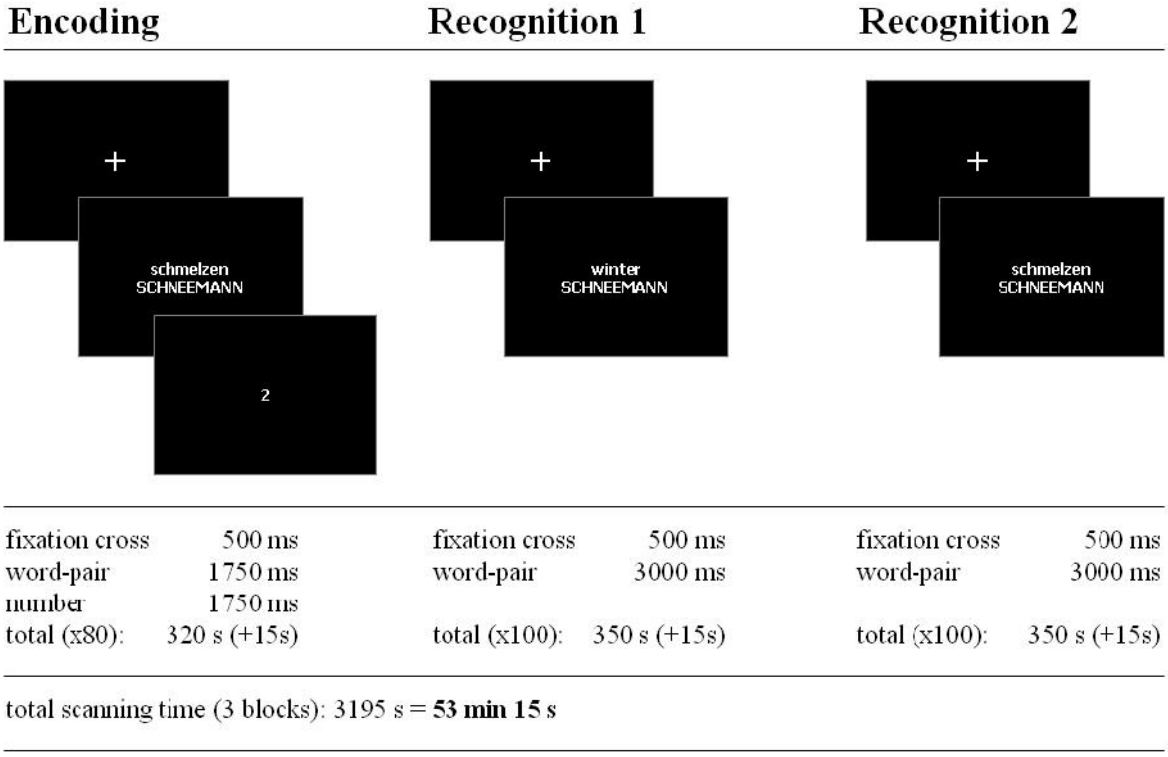

Figure 3: Experimental Paradigm: Duration times of fixation cross and item presentation. 15 s each were added to the total scanning time per session, representing lead in and lead out times of the scanner. No scanning took place during the filler task, which was excluded from this figure.

3.2.3.1. Encoding

During the encoding session, 80 word-pairs (AB) of weakly associated words were presented, (see appendix C for word list). The words were placed one above the other in the middle of the screen (white words against black background). The top word was printed in lower-case letters and the bottom word in upper-case letters, only. Participants were aware from the instructions that the bottom word represented the target and would have to be recognized later on. Upon presentation of the word-pairs, the participant's task was to decide weather or not the meaning of each word in the word-pair was subjectively easy to connect (association task). The presentation of each word-pair was followed by a single digit number, during which the participants were asked to indicate whether the presented number was odd or even. Figure 3 shows a visual summary of the paradigm. Before the presentation of each word-pair, a fixation cross was inserted for 500 ms. Word-pairs were visible on the screen for 1750 ms; numbers were shown for 1750 ms. A participant's failure to respond within the stimulus' presentation time led to a removal of the item from the analysis. The total time for one session of the encoding task was 5 min.

3.2.3.2. Comments on the Set-up of the Encoding Session

During the piloting phase of the experiment, it turned out to be essential to balance between total scanner time, encoding success and distribution of subsequent events for the behavioral and imaging analyses. A major consideration was the limitation of time each participant could remain in the scanner. Measures to decrease stimulus presentation time while increasing the strength of the behavioral effect were necessary to achieve the necessary number of events for analysis. After introducing the association task to initiate a deep level of processing during encoding, performance of pilot participants increased substantially. This led to the possibility of shortening encoding time per word-pair to a minimum, thus reducing overall scanning time. But the positive effect of this increased encoding performance was so strong that an additional distracter task (number task) had to be introduced to achieve an optimal distribution of ensuing behavioral events.

3.2.3.3. Filler Task

After encoding, a filler task of simple arithmetic equations was inserted to clear working memory. The equations were already solved and participants only had to indicate whether the proposed solution was correct or incorrect. The filler task lasted 3 min and 15 sec.

3.2.3.4. Retrieval 1

The first retrieval task consists of a recognition test in which the target word B was re-paired with a new word in a CB combination, thus changing the semantic context. The new context word (C) was selected for its close association to the target word (B). 100 word-pairs were presented, 80 target and 20 distracter pairs (XY). Participants were asked to read both words and decide if the second word (B or Y) had been previously presented in the encoding session ("old") or was presented for the first time ("new"). To ensure processing of the whole word-pair by the participant, the context words were placed in the same spatial position as the fixation cross. Between trials, participants focused on the spatial position where the context word is located during word presentation. The target word appears underneath the context word. Thus, processing of the context word precedes processing of the target word. Participants were asked to be absolutely sure if they decided to press the button for "old". Word appearance lasted for 2250 ms, and alternated with a fixation cross, which lasted for 1250 ms. Total scanning time amounted to 5 min 50 sec for each block.

3.2.3.5. Retrieval 2

In the second recognition test, the original word-pair combination (AB) was presented to the participant, thus reinstating the original encoding context. The same 20 distracters word-groups from retrieval 1 were used again, but a change was made from the previously strongly associated context word of the distracter to a weakly associated word (ZY). Participants read both words and indicate "old" if the presented word-pair was shown during the encoding task (old) or "new" if the word-pair was not among the encoded pairs. They were made aware that all words presented in the second position of the word-pairs (B or Y) had been shown before either during the encoding task (B) or as a distracter (Y) during the first retrieval session. This measure insured that for target-items, no novel stimuli were presented. Participants, also, had to differentiate if they recognized a target-item from the encoding list, or if the word presented was not part of the encoding list, but a distracter only presented at retrieval 1, reducing judgments based solely on familiarity. Again, word presentation lasted for 2250 ms and each word-pair presentation was followed by a fixation cross that remains on screen for 1250 ms, which resulted in a total testing time per block of 5 min 50 sec.

3.2.3.6. General Comments

In between sessions, a short break was used to repeat all vital instructions to the participants. Special emphasis was placed on the instruction that the participants should be absolutely certain when participants indicated that they recognized a word from the encoding session.

The total scanning time lasted 53 min 15 sec, the running time of the experiment, including all 4 tasks amounted to 63 min. Participants remained in the scanner between 90 and 120 min depending on the time spent on repetition of instructions and individual resting periods between blocks.

3.3. Imaging Parameters

Images were collected on a 3 Tesla Siemens Magnetom Trio (Siemens Medical Systems, Erlangen, Germany). For each participant an interleaved (bottom-up) echo-planar imaging sequence (TR = 3000 ms, TE = 30 ms, flip angle = 80°) was acquired. Jittering of volume acquisition was accomplished relative to item onset at 4000 ms during encoding and 3500 ms during recognition tests by using a TR of 3000 ms. 36 axial slices (128 x 96 voxels; voxel size = 2 x 2 x 3 mm) were acquired per repetition time with a total number of whole brain volumes of 112 for each encoding and 122 for each recognition session. These parameters lead to an image that does not encompass the whole brain. To achieve the desired time-space resolution, a part of the vertex of the brain was cut off in each participant. The cut-off was determined in the plane of the ac/pc-line by moving the scanning field to include all of the temporal lobe. After functional scanning, a high resolution T1-weighted anatomical image was created for each participant.

3.4. Preprocessing

Data preprocessing and statistical analysis were performed using statistical parametric mapping (SPM5, Wellcome Department of Cognitive Neurology, London, UK: www.fil.ion.ucl.ac.uk/spm/). Images were corrected for time acquisition to the middle slice prior to spatial modifications. Realignment to a mean image was completed before unwarping to correct for movement artifacts. Individual structural images were co-registered to the mean individual functional images followed by normalization to an average T1 template in a standard stereotactic MNI space (Montreal Neurological Institute, Montreal, Quebec, Canada: www2.bic.mmi.mcgill.ca) and re-sampled to 2 mm isotropic voxels. At last, images were smoothed with a Gaussian kernel of 6 mm at full-width of half maximum (FWHM).

3.5. Data Analysis

3.5.1. Single Subject Statistical Analysis

Event-related hemodynamic responses were modeled with delta stick functions at the onset of each event of interest, convolved with a first order canonical hemodynamic response function (HRF; Friston et al., 1995). Forming covariates from the resulting time series, three separate fixed effects general linear models were created – one model for the three encoding sessions, one for the first recognition test sessions and one for the three second recognition test sessions. For each of these three models, trials of interest were separated into four categories, items recognized across both tests (HH), items remaining unrecognized in both recognition tests (MM), items missed in retrieval 1 but correctly recognized during retrieval 2 (MH) and items correctly recognized in the first but missed in the second recognition test (HM). The models also included session-specific effects as separate covariates and six rigid-body movement parameters. A high-pass filter of 128 s was used to calculate statistical parametric maps of linear contrasts. The recognition test models included correct rejections and false alarm trials.

3.5.2. First-level Analysis

Contrast images of item-related activity against an implicit baseline were calculated for HH, MM and MH items. The HM category was disregarded, lacking the necessary number of events to allow for fMRI analysis in addition to being of minor theoretical interest.

3.5.3. Second-level Group Analysis

In a second level analysis a 3 x 3 repeated measure fully within-subject ANOVA was performed using the contrast maps from the first level analysis. The two factors of the ANOVA were defined by session type (encoding, retrieval 1, and retrieval 2) and item type (HH, MH, MM). Imaging results presented were calculated using simple t-tests within the ANOVA. Activity clusters with a minimum of 10 voxels and a statistical significant difference in brain activation at $p < 0.001$ (uncorrected) were listed in contrast tables unless otherwise specified.

The alpha-level for the behavioral analysis was set at 0.05. Easy_ROI (http://www.sbirc.ed.ac.uk/cyril/) was employed for the region of interest analysis and added to the SPM5 toolbox. ROI coordinates were selected by relevant contrasts between two item

types during the analysis. A univariate test for planned comparisons was used to determine significant differences between all item types

3.5.4. Contrasts of Interest

Specific contrasts between item types were assumed to represent certain neural correlates of episodic memory encoding, retrieval success and retrieval failure. For encoding, the contrast between MH and MM items represents context-dependent subsequent memory versus context-independent retrieval failure, while contrasting HH versus MM items defines the neural correlate of context-independent subsequent memory compared to retrieval failure. When contrasting MH versus HH items, difference in encoding activity for context-dependent versus context-independent subsequent memory was revealed.

At retrieval 1, neural correlates of forgetting may be explored. This stage of the experimental paradigm represents cued retrieval in a different context condition, manipulating semantic context by re-pairing target words with novel, closely associated stimuli. Thus, context-dependent compared to context-independent forgetting is examined in the contrast between MH versus MM items. Both item types were declared “new” by the participant.

At retrieval 2, the original context was reinstated on the screen, representing cued retrieval in a same context condition. Neural correlates of recognition memory for context-dependent as opposed to context-independent retrieval success were revealed.

For MH items, contrasts of hits versus misses at retrieval were disregarded from the experiment and remain unreported. Information about context dependence was confounded with retrieval success versus failure (MH versus HH) in the first recognition test and retrieval success versus failure (MH versus MM) in the second recognition test.

Within encoding and recognition tests and across retrieval, activity pattern for context-independent retrieval success versus forgetting were represented by contrasts between HH and MM items. This contrast was valuable to investigate established subsequent memory and retrieval effects. Comparison of context-independent retrieval effects across recognition tests were made in an interaction effect analysis. This interaction effect across tests for items successfully retrieved regardless of the context manipulation allows insight into the difference between cued retrieval processing for same and different context condition, testing the assumptions of the AtoM hypothesis for bottom-up and top-down attention to memory (Ciaramelli et al., 2008).

4. Results

4.1. Behavioral Data

4.1.1. Behavioral Results

Using the recognition failure of recognizable words paradigm, the main focus of this thesis was on imaging context dependency during encoding and retrieval and thus, finding neural correlates of context-dependent memory processes. To establish the neural correlates of this effect, participant responses to targets were categorized into 4 groups (see appendix D), depending on their value in retrieval 1 and retrieval 2. Targets recognized in the first and second recognition test were marked as Hit_Hit (HH) items (table 1). The Miss_Miss (MM) category includes targets unrecognized in both tests. Words were classed Hit_Miss (HM) item if they were remembered in the first test but later forgotten during the second. Words forgotten in the first but remembered in the second recognition test were placed into the Miss_Hit (MH) category. Missing, double, or out-of-time responses were discarded from the analysis. False alarm (FA) rates of the three blocks were added and separately noted for each retrieval test. The maximum number of false alarms for each recognition test was 60. Number of events for each category may be found in appendix D.

The 2x2 contingency table

		Retrieval 1	
		Hit	Miss
Retrieval 2	Hit	+ + (A)	- + (B)
	Miss	+ - (C)	- - (D)

Table 1: 2x2 contingency table. The events of hit or miss for each target-item during retrieval 1 and retrieval 2 are divided into four categories.

Proportions were calculated from the raw data for individual categories and presented along with their standard deviations in table 2 (p. 33).

Categories	Proportion	SD
HH	0.46	0.14
MH	0.24	0.07
HM	0.08	0.05
MM	0.17	0.10

Table 2: Proportion of overall events by category according to retrieval events. HH (hit-hit), MH (miss-hit), HM (hit-miss), MM (miss-miss), SD = standard deviation.

For a summary of hit rate (HTR), false alarm rate (FAR), sensitivity index (d') and response criterion (c) for retrieval 1 and retrieval 2 refer to table 3. The sensitivity index,

$$d' \text{ (d-prime)} = z(HTR) - z(FAR),$$

indicating recognition accuracy and the response criterion, tendency to say yes or no regardless of item status,

$$c = 0.5 * [z(HTR) + z(FAR)] ,$$

were calculated with adjusted values for hit and false alarm rates accounting for a lack of false alarms for certain participants. Corrections used were recommended by Snodgrass and Corwin (1988) and modified by Markopoulos (2005).

$$X_{modified} = ([X * 100) + 0.5] / 101$$

D'-values between 1 and 2 commonly indicate good yes-no recognition performance; a response criterion value greater than 0 suggests a conservative response bias, while a negative value hints toward a liberal criterion. A dependent t-test was applied to the d'-values

	HTR (SD)	FAR (SD)	d' (SD)	c (SD)
Retrieval 1	0.54 (0.12)	0.10 (0.05)	1.46 (0.39)	0.63 (0.31)
Retrieval 2	0.71 (0.13)	0.13 (0.11)	1.85 (0.67)	0.36 (0.40)

Table 3: hit rate (HTR) and false alarm proportions (FAR) for retrieval, SD = standard deviation in brackets, d' = sensitivity index, c = response criterion

and values for response criterion across retrieval tasks. The t-test for the sensitivity index indicates a significant difference between the two indices, $t_{(20)} = 4.05$, $p < 0.001$, thus showing that participants were better at distinguishing targets from distracters during the second recognition test. The t-test for the response criterion also reveals a significant difference between recognition tests, $t_{(20)} = 4.20$, $p < 0.001$. Response criterion was lower for recognition 2, indicating that participants were more inclined to say yes to a presented item than during recognition 1. This finding may be explained by the fact that participants were presented with the same distracters during retrieval 1 and retrieval 2, leading to a higher degree of familiarity for retrieval 2, despite the fact that recognition 2 should have been more difficult owing to the repeated distracters and longer retention interval. The second test had a greater temporal distance from the encoding task than the first retrieval test and all targets and distracter had been presented previously. Therefore, rather than, for example, relying on a feeling of novelty to differentiate between target and distracter, participants had to specifically remember the encoding episode.

Empirical Conditional Probability P(T1|T2) and the Standard Deviation STDIV

P(T1|T2) = 0.6456; STDIV = 0,1717.

The Tulving-Wiseman Function

$$P(Rn|Rc) = P(Rn) + c[P(Rn) - P(Rn)^2]$$
$$= P(T1) + 0.5[P(T1) - P(T1)^2]$$
$$= 0.6564$$

The value of the empirical conditional probability of retrieval during the first recognition test given retrieval during the second recognition test approaches the value calculated by the Tulving-Wiseman function. This confirms the adherence of the present study to the Tulving-Wiseman law within Gardiner's general contextual account for recognition failure of recognizable words.

4.1.2. Reaction Times

4.1.2.1. Encoding

Participants were given the associative task of judging the subjective ease of associability between context and target. Reaction times during incidental encoding were graphed in figure 4. Vertical bars denote 95% confidence interval.

A one-way within-subject ANOVA was used to calculate reaction times for encoding across item type. The ANOVA was significant, $F_{(2, 40)} = 11.81$, MSE = 0.01, $p < 0.001$. The Bonferroni corrected tests showed no significant difference between HH items and MH items for reaction times at encoding, $p = 0.712$, but between MM items and MH items a significant difference was found, $p = 0.004$. Thus, reaction times for encoding did not indicate later context-dependence versus independence but rather differentiated between subsequent memory and forgetting.

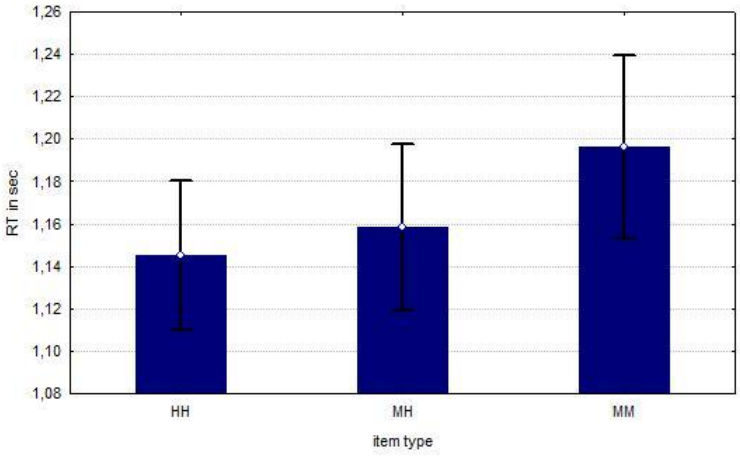

Figure 4: Reaction times for encoding: $F_{(2, 40)} = 11.811$; $p < 0.001$; HH: target-items subsequently recognized in both tests (hit-hit); MH: target-items missed during retrieval 1, but recognized during retrieval 2 (miss-hit); MM: target-items missed in both retrieval tests (miss-miss); RT = reaction time; vertical bars denote 0.95 confidence interval. Crosshairs indicate average reaction time.

4.1.2.2. Retrieval Tests

During two recognition tests, participants were asked to read both words and determine whether or not the second word in uppercase letters was presented during the encoding task. Reaction times for retrieval 1 and retrieval 2 were graphed in figure 5. Vertical bars denote 95% confidence interval. For both tests, one-way within-subject ANOVAs were calculated, respectively, $F_{(2, 40)} = 28.91$, MSE = 0.01, $p < 0.001$ and $F_{(2, 40)} = 58.17$, MSE =

0.01, p < 0.001, both were significant. For retrieval 1, further Bonferroni corrected tests revealed a significant difference in reaction times between HH items and MH items, p < 0.001 as well as HH items and MM items, but do not reach significance for MH items and MM items, p = 0.417. Thus, reaction times during retrieval 1 predict hits and misses for this specific recognition test, but do not predict subsequent hits or misses. Reaction times at retrieval 2 reach significance between all item types, Bonferroni corrected test for all comparisons between target-item types show a significance level of p < 0.001. Therefore, hits during retrieval 2 show a significant difference in reaction time for targets retrievable depending on the accompanying context (MH) and independent of context manipulations (HH).

The repeated measures 2 (tests) x 3 (item type) ANOVA between tests was not significant, $F_{(1, 20)} = 3.41$, MSE = 0.010, p = 0.080. For an overall comparison between tests, reaction times do not differ.

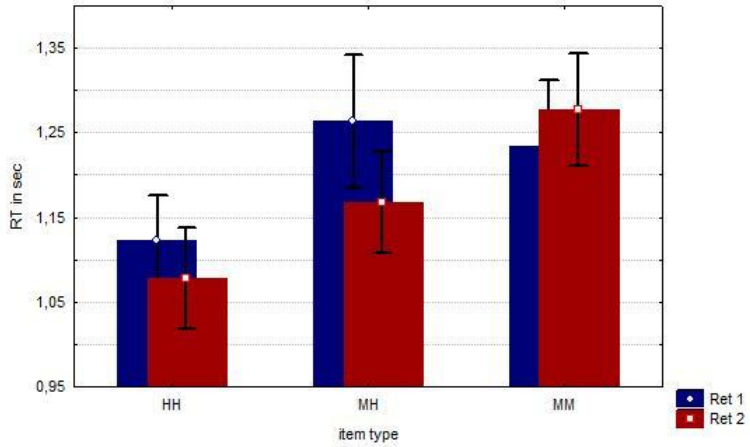

Figure 5: Reaction times for retrieval 1 (blue), $F_{(2, 40)} = 28.91$, MSE = 0.01, p < 0.001 and retrieval 2 (red), $F_{(2, 40)} = 58.17$, MSE = 0.01, p < 0.001 by target-item type: HH (hit-hit), MH (miss-hit), MM (miss-miss). RT = reaction time; Ret1 = retrieval 1; Ret2 = retrieval 2. Crosshairs indicate average reaction times. Vertical bars denote a 0.95 confidence interval.

4.2. Functional Imaging Data

Imaging results presented in this section focus on neural representation of retrieval failure of retrievable words, but also outline establish imaging patterns of common cognitive neuroimaging functions, including subsequent memory and retrieval success effects across encoding and two successive recognition tests. Additional information may be gained by comparing subsequent memory effects and retrieval success effects for context-dependent (MH) and context-independent (HH) target-items, respectively. Finally, novel information about controlled versus automatic retrieval processes may be established through comparison of the two retrieval tests for HH items in an interaction analysis. For these items, both tests involved successful recognition, but differential retrieval processing depending on the cue externally presented during the retrieval operation.

4.2.1. Encoding

4.2.1.1. Context-independent Subsequent Memory Effect – Enc: HH > MM

Brain activity during encoding contrasted according to events in subsequent recognition tests are shown in table 4 (p. 38). Differences during encoding of target-items remembered (HH) and target-items forgotten in both recognition tests (MM) demonstrates a classical hit-versus-miss pattern of activity. As expected for the experimental design, extensive activations were found for the HH > MM contrast. Retrieved items were later remembered independent of contextual manipulations and, consequently, demonstrate considerable memory strength. Major activations, predominantly on the left cerebrum, were elicited in bilateral inferior frontal gyrus (BA 47, 9, 45), bilateral medial frontal gyrus (BA 11) and left superior frontal gyrus (BA 8, 9). The inferior frontal areas were commonly labeled as ventrolateral prefrontal cortex (VLPFC), which includes the present activations in BA 47 and BA 45, and the dorsolateral prefrontal cortex (DLPFC), which was situated in the area around BA 9. Although only two activity peaks in this contrast were located in the right hemisphere, the strongest activation clusters in the frontal lobe were mirrored to a lesser degree in the right cerebrum. Additional activations were obtained from the left middle temporal gyrus and left angular gyrus (BA 39, 21), the left posterior cingulate gyrus (BA 23), left fusiform and inferior temporal gyrus (BA 20) and basal ganglia (putamen). In the area of the parahippocampal gyrus or hippocampus no activity was observed.

4.2.1.2. Context-dependent Subsequent Memory Effect – Enc: MH > MM

In a second comparison, the relationship between target-items forgotten in a different context during the first retrieval test but remembered when the context was reinstated during a second retrieval test (MH) were contrasted with items that were forgotten throughout the testing phase (MM). For this context-dependent subsequent memory effect at encoding, two contrasts were of theoretical value: Activity between context-dependent subsequent memory versus context-independent subsequent memory (Enc: MH > HH) and context-dependent subsequent memory versus context-independent subsequent forgetting (Enc: MH > MM), In the later contrast, notably less overall activation was found as compared to the context-independent subsequent memory effect (Enc: HH > MM). Activity clusters were sorted by significance. The strongest activity for MH > MM was again measured in predominantly left-lateralized inferior frontal gyrus (BA 47, 45) followed by activity in the bilateral anterior insular cortex (AIC), left middle temporal cortex (BA 21), and activity in bilateral thalamus as well as

Table 4: Subsequent Memory Effects: Activity during encoding; p < 0.001

Contrasts	Anatomical location	BA	Cluster size	t-value	MNI: x y z in mm
HH > MM	L. inferior frontal gyrus	47 / 9 / 45	931	7.37	-36 32 -10
	R. lentiform nucleus	Putamen	40	4.91	26 -10 10
	B. medial frontal gyrus	11	222	4.87	-6 46 -12
	L. angular gyrus / middle temporal gyrus	39	137	4.69	-40 -64 32
	L. posterior cingulate gyrus	23	90	4.48	-6 -52 16
	R. inferior frontal gyrus	47	77	4.41	32 34 -10
	L. middle temporal gyrus	21	27	4.37	-54 -12 -10
	L. superior frontal gyrus	8	115	4.11	-12 46 46
	L. fusiform gyrus	20	26	4.08	-28 -34 -22
	L. superior frontal gyrus	9	40	4.00	-12 54 28
	L. inferior temporal gyrus	20	89	3.91	-50 -56 -14
	L. middle temporal gyrus	39	24	3.81	-52 -70 26
MH > MM	L. inferior frontal gyrus	47	151	6.25	-34 32 -10
	R. insula (anterior)		29	4.64	42 8 -10
	L. inferior frontal gyrus	45	58	4.32	-54 28 6
	L. insula (anterior)		17	4.30	-40 2 -14
	L. middle temporal gyrus	21	60	4.08	-56 -52 -4
	B. thalamus		29	4.08	-2 -18 -4
	B. medial frontal gyrus	11	68	4.03	-2 40 -16
	L. medial frontal gyrus	6	19	4.01	-8 4 56
	R. inferior frontal gyrus	47	15	3.75	38 30 -12
MH > HH	L. superior temporal gyrus	21	43	4.57	-42 -12 -10
	R. insula (anterior)		20	4.10	38 12 12
	L. insula (anterior)		20	3.77	-44 6 -10
	L. precuneus	7	22	3.73	-8 72 42

bilateral medial frontal gyrus (BA 11, 6). Activations in the context-dependent subsequent memory versus context-independent forgetting contrast (Enc: MH > MM) largely seem to be a subset of areas also active in the contrast between context-independent subsequent memory and context-independent subsequent forgetting (Enc: HH > MM), except for the bilateral insular cortex and bilateral thalamus clusters.

4.2.1.3. Context-dependent versus Context-independent Subsequent Memory – Enc: MH > HH

The second subsequent memory effect contrasting context-dependent target-items was measured between context-dependent subsequent memory versus context-independent subsequent memory (Enc: MH > HH). The difference between these target-item types at encoding essentially represents the difference in neuronal processing at encoding for targets susceptible to forgetting due to contextual change versus targets that remain recognizable despite the change in cue during retrieval (different context condition). When contrasting context-dependent subsequent memory with context-independent subsequent memory, only four mostly left-lateralized areas became significant: left superior temporal gyrus (BA 21), left precuneus (BA 7), and bilateral anterior insular cortex (see table 4).

4.2.1.4. Region of Interest Analysis at Encoding: MH > MM

Areas of interest were selected from the context-dependent subsequent memory contrast (MH > MM) to remove context-independent successful encoding activity from this particular analysis (table 4, p. 38, activity peaks marked in blue). Here, two different types of forgetting were contrasted to show difference in activity pattern that resulted in the same behavioral decision but underwent separate neuronal pathways to reach this decision. Essentially, one may also describe this encoding activity as subsequent context-dependent forgetting versus subsequent context-independent forgetting. First eigenvariates were calculated for each area and presented alongside the corresponding brain images in figure 6 (a – c, p. 40). For these areas a significant difference in activity was obtained for context-dependent subsequent memory and context-independent forgetting. Of all clusters, the left inferior frontal gyrus (BA 47, cluster size: 151, $t_{(20)} = 6.25$, MNI (x y z): -34 32 10, $p < 0.001$; figure 6 a (p. 40) was chosen due to its common link to successful memory encoding to compare to areas unique to the context-dependent subsequent memory effect. For bilateral thalamus activity (cluster size: 29, $t_{(20)} = 4.08$, MNI (x y z): -2 -18 -4), right anterior insular cortex (cluster size: 29, $t_{(20)} = 4.64$, MNI (x y z): 42 8 -10, $p < 0.001$; figure 6 b (p.40) and left anterior insular cortex (cluster size: 17, $t_{(20)} = 4.30$, MNI (x y z): -40 2 -14, $p<0.001$; figure 6 c (p. 40) as well as inferior frontal gyrus first eigenvariates were extracted for each target-item type. Figure 6 (a – c, p. 40) presents results for insular and frontal clusters.

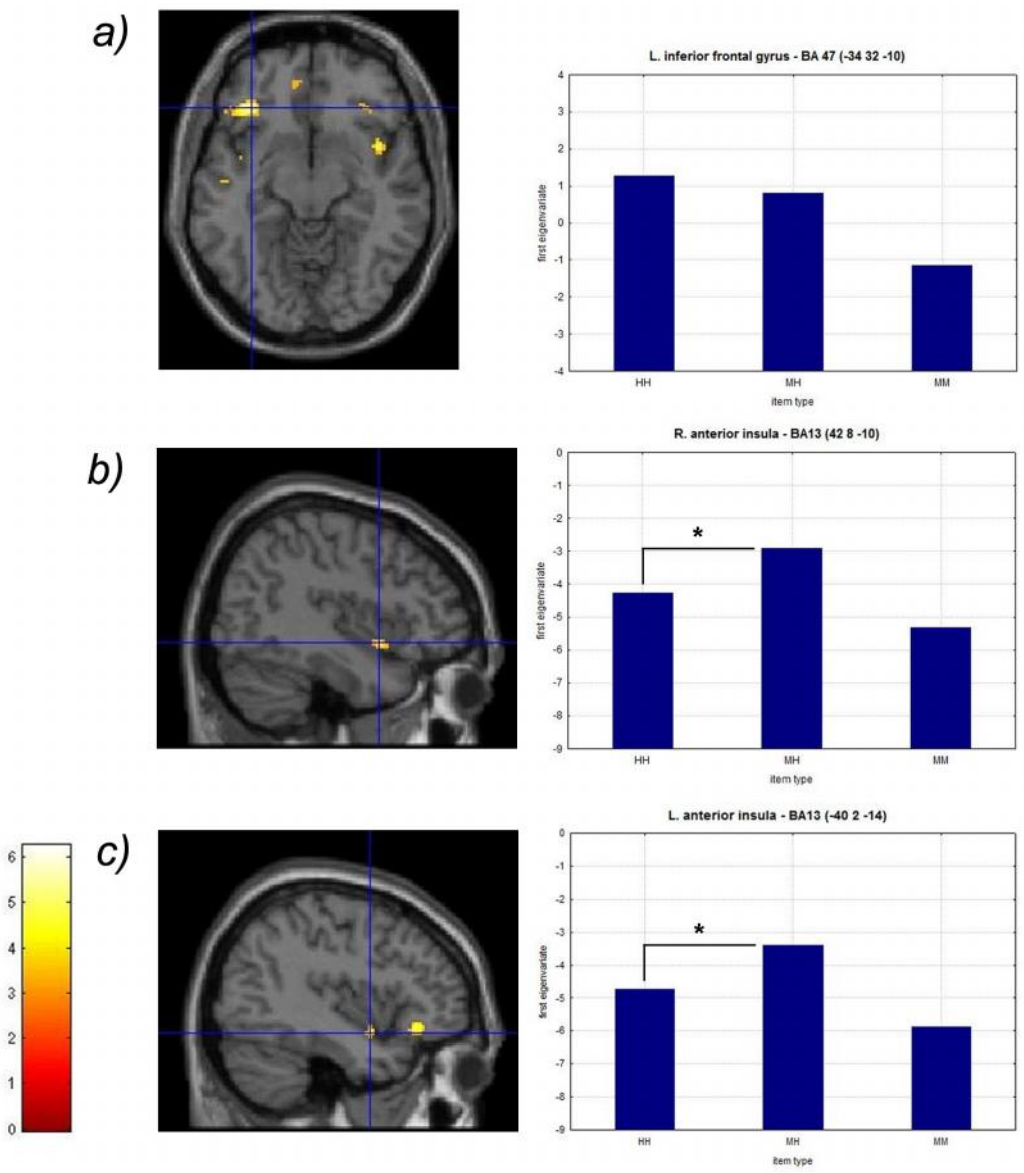

Figure 6: ROI Analysis for Encoding Activity: MH > MM;, p < 0.001. Corresponding clusters are presented on average brain image template. Bar plots represent the first eigenvariates extracted from the activation cluster in: a) left inferior frontal gyrus b) right anterior insular cortex and c) left anterior insular cortex. Crosshairs indicate peak activation. For a dependent t-test between item types, the asterisk denotes a significant difference in activity.

A dependent t-test was used to show differences between context-dependent subsequent memory and context-independent subsequent memory in these clusters. There was no difference between HH and MH items in the left inferior frontal gyrus (BA 47), $t_{(20)}$ = 1.69, p = 0.107, or in the thalamus clusters, $t_{(20)}$ = 0.959, p = 0.349. Consequently, left inferior

frontal gyrus and thalamus do show a subsequent memory effect, but they do not discriminate between context-dependent and context-independent subsequent memory effects. For the insular clusters a significant difference was found in the right anterior insular cortex, $t_{(20)} = 2.43$, $p = 0.025$, and the left anterior insula cortex, $t_{(20)} = 2.32$, $p = 0.031$. Accordingly, of all areas investigated in the region of interest analyses, only insular cortex activity was greater for MH items compared with the other two item types.

4.2.1.5. Conjunction Analysis between MH > MM and MH > HH at Encoding

Performing a conjunction analysis between MH > MM and MH > HH (α-level = 0.005 for clarity, voxel-extent threshold: 10) only two clusters were found to have common activations in both contrast. One cluster was located in the right anterior insular cortex (cluster size: 30, $t_{(20)} = 3.57$, MNI (x y z): 42 8 -8) and the other was located in the left anterior insular cortex (cluster size: 32, $t_{(20)} = 3.14$, MNI (x y z): -42 2 -12).

Thus, the anterior insular cortex was the only area more active for target-items encoded in a manner that leads to context-dependent subsequent memory (MH) as opposed to context-independent subsequent memory (HH) and context-independent forgetting (MM).

4.2.2. Retrieval 1

4.2.2.1. Context-independent Retrieval Success versus Forgetting – Ret1: HH > MM

Target-items remembered during retrieval 1 were recognized independent of context and reflect high memory strength. When contrasted with targets that were forgotten independent of context, for example, on account of insufficient encoding, essentially, retrieval success for context-independent target-items remains (Ret1: HH > MM). For all results from this contrast, refer to table 5 (p. 42). Widespread activations were detected in parietal lobule, including precuneus, which were predominantly left-lateralized (BA 7, 40), bilateral middle temporal gyrus (BA 37, 21), left-lateralized frontal lobe (BA 6, 9, 11, 8) and bilateral inferior frontal gyrus (BA 47), which are classic retrieval success areas.

4.2.2.2. Context-dependent versus Context-independent Forgetting – Ret1: MH > MM

Table 5 (p. 42) reports activity during encoding that was found for target-items forgotten during the first retrieval test but remembered in the second as opposed to activity elicited by target-items forgotten in both successive recognition tests (Ret1: MH > MM). This contrast cites differential activity for two types of targets which were both forgotten during retrieval 1. Fewer and far less widespread activations for this contrast were found, chiefly in bilateral superior (BA 8, 6)

and left inferior frontal gyrus (BA 47). Additional activity was obtained in bilateral anterior insular cortex and left parahippocampal gyrus (parahippocampal cortex, BA 35).

Table 5: Activity at Retrieval 1; p < 0.001

Contrasts	Anatomical location	BA	Cluster size	t-value	MNI: x y z in mm
HH > MM	L. superior/inferior parietal lobule	7/40	1563	6.84	-36 -62 52
	R. middle temporal gyrus	37/21	100	5.69	56 -48 -8
	L. middle frontal gyrus	6/9	807	5.35	-46 2 52
	L. precuneus	7	391	5.30	-6 -66 42
	L. middle frontal gyrus	11	97	5.02	-44 48 -10
	L. inferior frontal gyrus / insula (anterior)	47	95	5.00	-34 20 -4
	R. superior parietal lobule	7	739	5.00	32 -70 56
	R. inferior parietal lobule	40	82	4.45	46 -46 60
	R. declive	Cerebellum	39	4.29	8 -78 -28
	R. declive	Cerebellum	47	4.28	32 -66 -30
	L. middle temporal gyrus	21	47	4.18	-56 -34 -8
	L. superior frontal gyrus	6	20	4.02	-22 12 56
	L. medial frontal gyrus	8	28	3.91	-2 22 50
	L. caudate	Body	22	3.86	-12 10 8
	R. inferior frontal gyrus	47	18	3.66	36 20 -2
	L. caudate	Body	15	3.64	-12 2 20
MH > MM	L. inferior frontal gyrus	47	69	4.88	-30 22 -6
	L. insula (anterior)		64	4.45	-40 12 2
	L. superior frontal gyrus	8	15	4.35	-6 20 56
	R. superior frontal gyrus	6	22	3.93	4 12 56
	R. insula (anterior)		74	3.90	40 16 6
	L. parahippocampal gyrus (parahippocampal gyrus)	35	22	3.70	-22 -26 -16

4.2.2.3. Region of Interest Analysis at Retrieval 1: MH > MM

A region of interest analysis was performed on relevant areas active in the MH > MM contrast at p < 0.001 during retrieval 1 to determine differences in activity level among all target-item types. Although both target-types are declared “new” by participants, the former would be remembered later, when the original cue was reinstated during retrieval 2 (same context condition). First eigenvariates for each focus (table 5, activity peaks marked in blue) were extracted by item type and are displayed in figure 7 (a – d, p. 44) along with the equivalent cluster on a brain image. Selected areas were located in left inferior frontal gyrus (BA 47, cluster size: 69, $t_{(20)}$ = 4.88, MNI (x y z): -30 22 -6; figure 7 a, left anterior insular cortex (cluster size: 64, $t_{(20)}$ = 4.45, MNI (x y z): -40 12 2; figure 7 b (p. 44), right anterior insular cortex (cluster size: 74, $t_{(20)}$ = 3.90, MNI (x y z): 40 16 6; figure 7 c, and left parahippocampal cortex (BA 35, cluster size: 22, $t_{(20)}$ = 3.70, MNI (x y z): -22 -26 -16; figure 7 d (p. 44). For this contrast targets were missed in both groups of events. Misses for MH

items may reflect forgetting due to a change of context, while misses for MM items were assumed to be forgotten for reasons unrelated to context. Dependent t-tests for HH and MH items were performed for all clusters. There was no significant difference between HH and MH items activity in the left inferior frontal gyrus, $t_{(20)} = 0.58$, $p = 567$, and left parahippocampal gyrus cluster, $t_{(20)} = 1.41$, $p = 0.174$. These clusters do seem to differentiate between retrieval success and context-independent forgetting, but they do not account for differences between context-dependent and context-independent retrieval success. Activity in these areas reflects successful memory retrieval independent of context manipulation. A difference for HH and MH items were observed for the left anterior insular cortex activity, $t_{(20)} = 2.59$, $p = 0.031$, and approached significance for right anterior insular cortex, $t_{(20)} = 2.07$, $p = 0.052$.

One other cluster in the context-dependent retrieval success versus context-independent forgetting contrast mimicked the insular activation pattern, which was not anticipated in this analysis. The right superior frontal gyrus also showed a significant difference between HH and MH items at retrieval 1, $t_{(20)} = 2.28$, $p = 0.033$.

Thus, during retrieval 1, the AIC shows differential activity for target-items recognized independent of context, items that were only recognized in a context-dependent manner, and targets forgotten for other reasons than change of context. Critically, the AIC was most active for target-items forgotten due to context change.

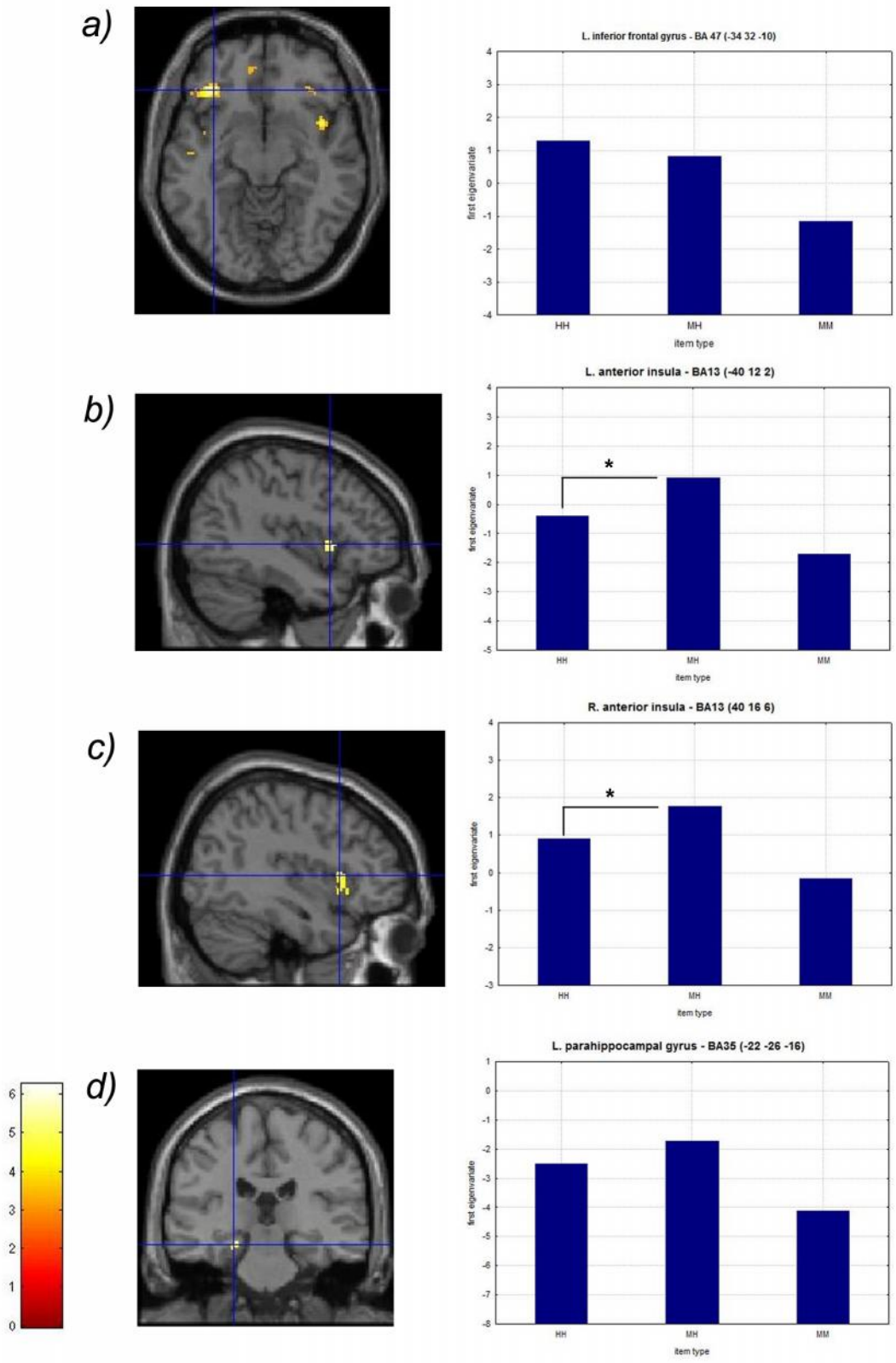

Figure 7: ROI-Analysis of Retrieval 1 Activity: MH > MM by item type; p < 0.001. Corresponding activity clusters are presented on brain images. Bar plots represent the first eigenvariates extracted from the activation cluster in a) left inferior frontal gyrus b) left anterior insular cortex c) right anterior insular cortex and d) left parahippocampal gyrus (perirhinal cortex). Crosshairs indicate peak activation. For a dependent t-test between item types, the asterisk denotes a significant difference in activity.

4.2.3. Retrieval 2

4.2.3.1. Context-independent Retrieval Success versus Forgetting – Ret2: HH > MM

In the HH > MM imaging contrast (table 6), activity was contrasted based on both prior and present retrieval success. Target-items previously remembered in a recognition test and successfully retrieved in a second recognition test were compared to items forgotten throughout the testing phase. The main activations for this contrast were situated in the brain's median plane around the area where the parietal lobe borders on the limbic lobe and where the parietal lobe touches onto temporal lobe around the lateral surface. In the median plane, large activation clusters were located bilaterally in the paracentral lobule, posterior

Table 6: Activity at Retrieval 2; p < 0.001

Contrasts	Anatomical location	BA	Cluster size	t-value	MNI: x y z in mm
HH> MM	L. paracentral lobule	31	278	4.90	-4 -34 46
	L. medial frontal gyrus	10	559	4.85	-4 60 8
	L. precuneus	31	65	4.39	-22 -68 22
	R. precentral gyrus	4	64	4.38	30 -34 60
	L. precuneus	39	173	4.31	-38 -68 32
	L. culmen	Cerebellum	47	4.30	-12 -42 -14
	L. superior temporal gyrus	39	115	4.26	-46 -56 18
	R. superior temporal gyrus	39	85	4.26	44 -58 20
	L. middle temporal gyrus	21	14	4.15	-56 -28 -16
	R. posterior insula	13	78	4.14	36 -18 12
	R. precuneus	31	145	4.12	20 -62 22
	L. parahippocampal gyrus	Hippocampus	75	4.06	-30 -20 -20
	R. middle temporal gyrus	39	11	3.99	54 -56 4
	L. cingulate gyrus	24	31	3.96	-4 -4 38
	R. medial frontal gyrus	11	20	3.93	8 30 -12
	L. precuneus	7	61	3.93	-2 -56 46
	R. precuneus	7	77	3.91	18 -80 50
	L. posterior cingulate gyrus	29	45	3.85	-6 -52 4
	L. posterior cingulate gyrus	31	27	3.80	-12 -54 18
	R. caudate	Head	12	3.77	8 14 -2
	L. superior frontal gyrus	8	14	3.74	-20 22 54
	R. inferior temporal gyrus	37	16	3.64	58 -56 -4
	R. precuneus	19	34	3.58	34 -78 38
	L. posterior insula	13	15	3.47	-54 -36 18
	L. anterior cingulate gyrus	24	10	3.40	-4 36 4
	R. parahippocampal gyrus (parahippocampal cortex)	35	11	3.34	20 -30 -12
MH > HH at P < 0.005	L. insula (anterior)		20	3.27	-34 24 2
	R. insula (anterior)		15	3.23	36 18 8

cingulate and precuneus (BA 31, 7), stretching along the bilateral anterior cingulate (BA 24) towards the bilateral medial frontal gyrus (BA 10, 11). Right prefrontal gyrus (BA 4) and a small cluster in the left superior frontal gyrus (BA 8) were the only other frontal areas in this contrast. In the more lateral sagittal plane, predominantly bilateral activations were spread out in several separate clusters between precuneus (BA 31, 39) and right inferior temporal gyrus (BA 37) towards superior and middle temporal gyrus (BA 19, 39, 22 and 21). In addition to cingulate activity, other limbic regions show differential activity, including left hippocampus and right parahippocampal gyrus (parahippocampal cortex, BA 35). Again, all clusters cited are part of classic retrieval success areas. Interestingly, bilateral posterior insular cortex (BA 13) activations were also revealed in the HH > MM contrast.

4.2.3.2. Context-dependent versus Context-independent Retrieval Success – Ret2: MH > HH

After looking at retrieval success versus forgetting (Ret2: HH > MM), a second contrast was calculated that essentially investigates context-dependent versus context-independent retrieval success (Ret2: MH > HH) depending on prior retrieval success for recognizable target-items (table 6, p. 45). Correctly recognized targets previously susceptible to context-dependent forgetting were compared to recognized items insensitive to context-dependent forgetting. This set-up distinguishes differences in brain activation for past events. Essentially, the difference in activity depends on what participants decided during the first recognition test, and thus, reflects a somewhat differential previous processing pattern for context-dependent (MH) and context-independent target-items (HH). Since this contrast demonstrates a difference of what had happened to the item in the past, this contrast could be expected to reveal brain areas uniquely associated with remembering due to a reinstated context. Activity was only found for a lower level of significance at $p < 0.005$, perhaps representing the measurable but subtle effect previous processing exercises on subsequent processing activity. Clusters in the left inferior frontal gyrus (BA 47) and bilateral anterior insular cortex were extracted for this contrast. The cited areas showed a higher level of activity for context-dependent as compared to context-independent retrieval.

4.2.3.3. Region of Interest Analysis at Retrieval 2: MH > HH

Finally, a region of interest analysis was performed for activity in the MH > HH contrast during retrieval 2 (table 6, p. 45, activity peaks marked in blue). This analysis demonstrates differences in processing activity between all target-item types for a specific brain area. Clusters in the bilateral anterior insular cortex were the only significant activity in this contrast set at $p < 0.005$. Both item types were correctly recognized during retrieval 2. The sole difference between these items was their fate at retrieval 1, when targets were

either missed due to context-dependent forgetting or remembered due to context-independent recognition. For each cluster first eigenvariates were calculated by item type and graphed in figure 8 (a – b) next to the corresponding brain image of the area.

Once more, dependent t-tests were calculated for MH and MM item first eigenvariates in both clusters. Both were significant, for left anterior insular cortex, $t_{(20)} = 3.155$, $p = 0.005$, figure 8 a, and for right anterior insular cortex, $t_{(20)} = 3.72$, $p = 0.001$ (figure 8 b).

A linear pattern was found for insular activity between HH, MH and MM items. Target-items showing recognition failure independent of context present with the highest insular activity (MM), followed by items recognizable depending on the presented context (MH), and target-items that were recognizable independent of contextual manipulations (HH).

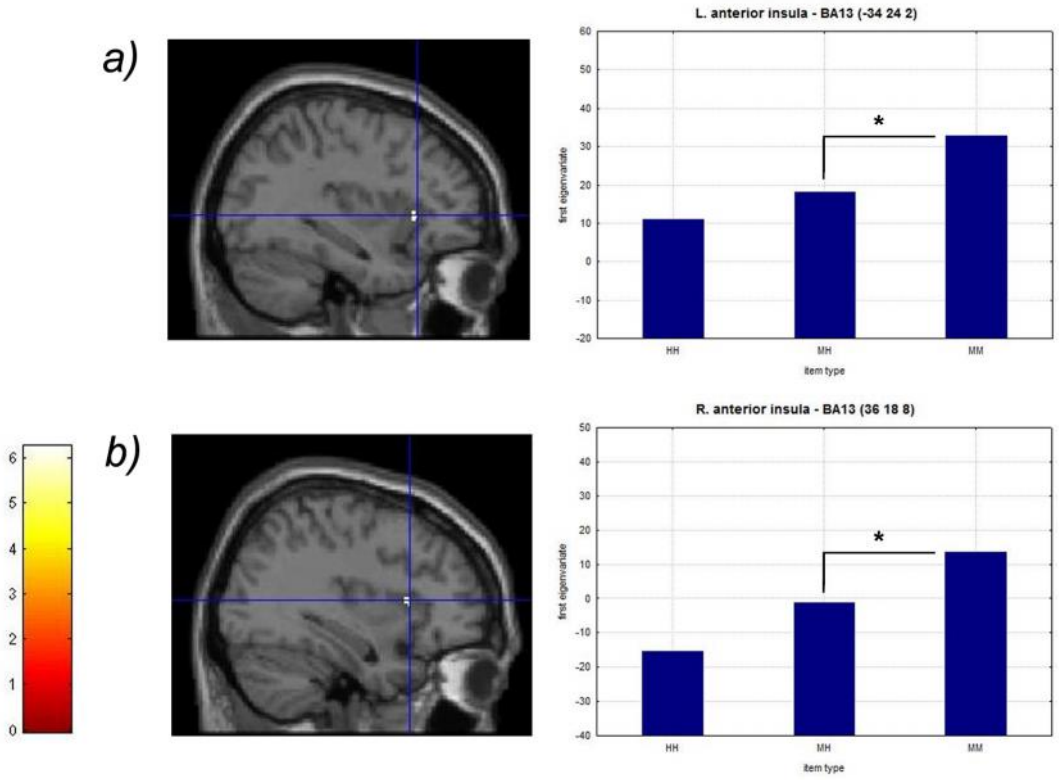

Figure 8: ROI Analysis of Retrieval 2 Activity: MH > HH; p < 0.005. Corresponding clusters are presented on brain images. Bar plots represent the first eigenvariates extracted from the activation cluster in: a) left anterior insular cortex and b) right anterior insular cortex. Crosshairs indicate peak activation. For a dependent t-test between item types, the asterisk denotes a significant difference in activity.

4.2.4. Interaction Effect between Retrieval 1 and Retrieval 2 for Context-independent Retrieval Success versus Forgetting

Using an interaction analysis approach, differences across the two recognition test were demonstrated for particular activation patterns (HH > MM; table 7). Differences in these two consecutive tests were significant for frontal and parietal lobe activity. Active frontal areas were located in and around the bilateral inferior frontal and left middle frontal gyrus (BA 47) extending into the bilateral anterior insular cortex as well as the left medial (BA 8) and right middle frontal gyrus (BA 9). Parietal activity was obtained in bilateral inferior parietal lobule (BA 40).

Table 7: Interaction Effect Analysis between HH > MM at Retrieval 1 & Retrieval 2; p < 0.001

Contrasts	Anatomical location	BA	Cluster size	t-value	MNI: x y z in mm
Inter-action effect	L. inferior frontal gyrus / insula (anterior)	47	1577	6.20	-30 22 -4
	R. inferior frontal gyrus / insula (anterior)	47	207	5.28	38 20 0
	L. inferior parietal lobule	40	542	4.86	-42 -56 54
	L. middle frontal gyrus	47	61	4.83	-46 46 -8
	L. medial frontal gyrus	8	341	4.64	-4 26 50
	R. inferior parietal lobule	40	95	4.60	38 -54 52
	R. declive	Cerebellum	17	3.89	10 -78 -28
	R. middle frontal gyrus	9	22	3.78	38 18 38
	R. middle frontal gyrus	9	33	3.68	36 24 26

Two specific cortical areas relevant to the different types of retrieval tests were selected for further analysis. The left inferior parietal lobule (figure 9, p. 49), an activity cluster close to the superior attentional system mediating top-down attentional processes to memory (Ciaramelli et al., 2008) and the left inferior frontal gyrus (VLPFC, BA 47; figure 10, p. 49) which is thought to be associated with cue selection, a control process necessary for the specification of the retrieval process, for example, orientation to the retrieval cue (Simons, Gilbert et al., 2005). Badre et al. (2005) concluded that the left anterior VLPFC (BA 47) is concerned with retrieval of semantic knowledge through top-down controlled mechanisms accessing long-term memory representations in the lateral temporal region. Dependent t-tests were used to show differences between target-item types across recognition tests.

First, differences between item types within recognition tests were calculated. As expected from the interaction effect analysis, at retrieval 1, both the left inferior parietal lobule and the left inferior frontal gyrus showed preferential activity for HH-items as compared to MM-items, $t_{(20)} = 4{,}86$, $p < 0.001$ and $t_{(20)} = 6.20$, $p < 0.001$ respectively. For retrieval 2, the

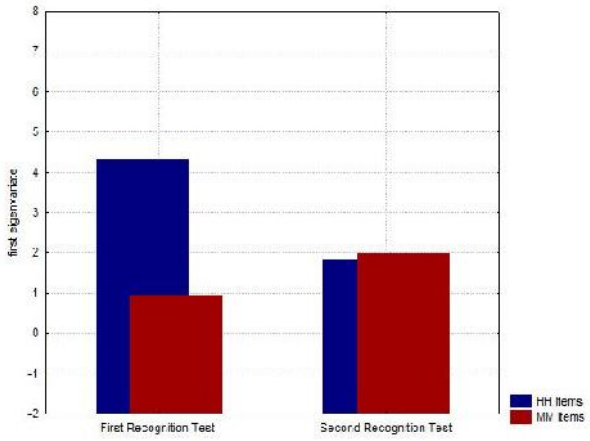

Figure 9: ROI Analysis for the Left Inferior Parietal Lobule (BA 40; MNI (x y z): -42 -56 54) across Recognition Tests: First eigenvariates were extracted for HH (hit-hit) items and MM (miss-miss) items for each recognition test. Crosshairs indicate peak activation.

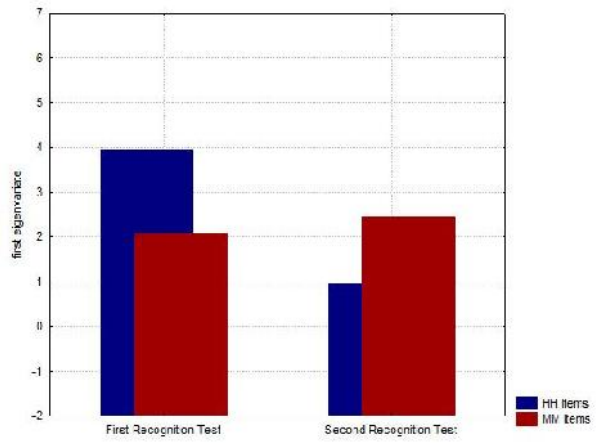

Figure 10: ROI Analysis for the Left Inferior Prefrontal Cortex (VLPFC, BA 47; MNI (x y z): -30 22 4) across Recognition Tests: First eigenvariates were extracted for HH (hit-hit) and MM (miss-miss) items for each recognition test. Crosshairs indicate peak activation.

activity pattern changed. Within the left inferior parietal lobule no difference between recognized and forgotten targets may be detected, $t_{(20)} = 0.228$, $p = 0.822$ (figure 9: ROI). But for the left inferior frontal gyrus (VLPFC, BA 47; figure 10: ROI), at retrieval 2, increased activity was elicited by MM target-items in the left inferior frontal gyrus compared to HH target-items: $t_{(20)} = 3.32$, $p = 0.003$. To further analyze the relationship between item types and retrieval tests for the left inferior frontal gyrus comparisons within item type but between tests were measured. For HH target items between recognition tests, the VLPFC was

preferentially active for successful retrieval of HH target-items during retrieval 1 as compared to retrieval 2: $t_{(20)} = 3.85$, $p = 0.001$. There was no difference between MM target-items across the two recognition tests: $t_{(20)} = 0.454$, $p = 0.655$. Thus, for target-items forgotten for reasons unrelated to the contextual manipulation, activity levels for the VLPFC did not differ between recognition tests.

5. Discussion

The discussion will first focus on the present study's novel approach of imaging context-dependent encoding and retrieval memory before comparing the acquired activation clusters to common activation patterns for encoding and recognition memory. Special attention is directed to comparisons between retrieval operations. This particular auxiliary comparison was possible through the specific sequence of testing required to image context-dependent memory.

The second major section of the discussion will focus on neural correlates of context-dependent memory and the role of the anterior insular cortex for encoding and recognition memory. To establish a role of the anterior insular cortex in memory, an extensive literature research is conducted to find previous citations of insular activity in memory paradigms. No paradigm including a priori insular cortex activity predictions for memory paradigms existed at the time this study was designed. The anterior insular cortex was previously associated with awareness and was recently implicated as a major module of cortical connectivity networks previously predominately associated with attention and executive functions, but also supporting memory operations. Lastly, a link connecting awareness, attention, and episodic memory will be established.

5.1. The Incidental Influence of Context on Memory

Numerous imaging studies have investigated episodic memory and context using the remember/know procedure, source memory, confidence ratings, the amount of information recollected, or associative memory. The common denominator for all of these approaches is that participants are explicitly asked to remember the encoded context during retrieval. Responses may be a specific detail from the study event, for example, when, where or how an item was presented, a remember/know response, a subjective judgment of memory strength for an item or a simple yes-no answer (Yonelinas, 2002; Diana et al., 2007). In the present study the incidental influence of semantic context on item memory encoding and retrieval is examined. At encoding, a word-pair is learned in an incidental fashion using an associative task. During both stages of testing, participants are required to provide a yes-no memory judgment on the provided target. They are not instructed to remember the accompanying semantic context, but only "to read both words of the word-pair and determine if the second word (target) was presented during learning." Participants are not directly asked to encode or provide the context for a target.

Episodic recognition has frequently been divided into categories including recollection and familiarity, or source memory, and item memory (contrasted against misses). Recollection and familiarity were determined by remember/know judgments (Otten, 2007) and/or a recognition confidence rating (Montaldi et al., 2006). The incidental approach allows for a categorization of context-dependent and context-independent items by what happens during two successive memory tests. Target-items always remembered despite the context change during the first recognition test (HH) are assumed to be context-free, while items are assumed to be context-bound when recognized only after the context is reinstated in the second recognition test (MH). These assumptions are drawn from theories explaining the recognition failure of recognizable words effect (e.g. The Contextual Account, Gardiner, 1994; The TECO Theory, Sikström, 2000). Despite being successfully encoded, targets fail to be recognized, because the cue (context and target) presented at retrieval is unable to trigger the memory trace. In the Encoding Specificity Principle, Tulving (1974) called this occurrence of retrieval failure cue-dependent forgetting.

In the present experiment the behavioral data suggest recognition failure of recognizable words for a significant proportion of retrievable targets. Of all presented target-items, 70% were successfully recognized in the second recognition test, while only 54% were remembered during the first recognition test. False alarm rates were also taken into account using the sensitivity index d'. These results suggest superior recognition performance for retrieval 2. This advantage in performance was found regardless of the increased temporal distance to encoding for the second recognition test and the fact that participants had to distinguish between targets and previously presented and thus familiar distracters. Considering reaction times, participants spent significantly longer on MH target-items at retrieval 1, when they were missed, than at retrieval 2, when targets were remembered, despite the fact that they had previously declared these target-item to be new. Therefore it is reasonable to argue that context reinstatement is a probable reason for superior performance at retrieval 2.

Another possible interpretation of the behavioral results may be by explaining the better performance in terms of accessibility and availability. Target-items that were missed in the first test, but remembered in the second (MH) may be available but temporally inaccessible. Habib and Nyberg (2008) ran an experiment in which encoding was followed by two retrieval tests, a cued recall and an associative recognition test. Participants indicated whether or not the word-pair was related, before retrieval was tested with cued recall (original cue) followed by associative recognition. During the associative recognition task, participants were asked to judge if a word-pair was intact or recombined (original cue and target versus novel cue and target). Critically, in contrast to the present study, retrieval performance between the successive retrieval tests did not differ and no context

manipulation was conducted. Furthermore, the terms accessibility and availability are only descriptive in nature. They describe the results of a retrieval tasks but offer no causal explanation for the behavioral effect. These facts contradict the accessibility and availability interpretation of the present behavioral data and support the contextual account.

5.2. Neural Correlates of Contextual Processing during Encoding

Difference in encoding activity for context-dependent and context-independent targets may aid understanding of the later behavioral effect of recognition failure of recognizable words. Two subsequent memory effects have been investigated in this study, context-independent hits versus context-independent misses (Enc: HH > MM) and context-dependent hits versus context-independent misses (Enc: MH > MM). An additional contrast investigates a subsequent memory effect by comparing context-dependent hits versus context-independent hits (Enc: MH > HH).

5.2.1. Context-independent Subsequent Memory Effect

When contrasting context-independent retrieval success versus context-independent retrieval failure (Enc: HH > MM) during encoding, the list of activations found overlaps considerably with results obtained from a meta-analysis of subsequent memory effects by Spaniol et al. (2009). The largest clusters in terms of size and statistical value were elicited in the left inferior and middle frontal gyrus.

The first cluster positioned around the ventrolateral prefrontal cortex (VLPFC; BA 47, 45), which has been associated with selection (or rather controlled retrieval) and maintenance of semantic information, essentially functioning as a semantic working memory system (Blumenfeld & Ranganath, 2007; Badre et al., 2005; Poldrack et al., 1999; Wagner et al., 2001). Further differentiation was proposed by Badre et al. (2005), suggesting that the anterior VLPFC is concerned with controlled retrieval of semantic information, while mid-VLPFC operates during post-retrieval selection to resolve competition among retrieved information. Anterior VLPFC activity is also commonly linked to left middle temporal gyrus activity (BA 21), in order to retrieve semantic knowledge from long-term memory (Bokde et al., 2001, Dobbins & Wagner, 2005). Activity in all of these areas is modulated by associative strength (Badre et al., 2005).

The second cluster was located in the dorsolateral prefrontal cortex (DLPFC; BA 9); activity in DLPFC is not always found for subsequent memory effects. For both prefrontal areas, greater activity was found for relational encoding than item-specific encoding by

Murray and Ranganath (2007). But compared to the VLPFC, which was found to predict both successful memory for associations and items, the dorsolateral prefrontal cortex was only linked to successful memory formation of associations in their study (Murray & Ranganath, 2007). Thus, DLPFC seems to be preferentially active when the relationship between encoding items is stressed and consciously processed by the participant. In the present study, participants were asked to rate the associability of the word-pairs presented, thus encouraging them to assess the relationship between context-word and target-word.

Left-lateralized activity clusters in the area of the temporoparietal junction near the angular gyrus (BA 39) were also detected preferentially for the context-independent subsequent memory effect (Enc: HH > MM). These areas are associated with semantic processing (Binder et al., 2009).

No activations were observed around the medial temporal lobe during encoding, despite the fact that hippocampal and parahippocampal activity is found in the meta-analysis by Spaniol et al. (2009). There is no clear reason why MTL activity is sometimes not found for subsequent memory effects, especially for semantic material. For a discussion on failure to obtain MTL activity for subsequent memory effects, refer to Henson (2005).

5.2.2. Context-dependent Subsequent Memory Effect

Further analysis was conducted on the encoding data in terms of investigating the subsequent memory effect for context-dependent retrieval success versus context-independent retrieval failure (Enc: MH > MM). Given that targets in this contrast were only remembered during the second recognition test, when the context was reinstated, and the fact that the number of events for MH target-items was restricted compared to HH items, less extensive activations were expected. As presented in table 4 (p. 38), clusters found in the context-dependent contrast overlap with clusters found in the context-independent retrieval success versus failure contrast (Enc: HH > MM), except the bilateral anterior insular cortex (AIC) cluster. Although the bilateral thalamus activation was not found among the activity clusters in the context-independent contrast, a region of interest analysis did not confirm a pattern analog to AIC activity. The small thalamus effect may not have reached statistical significance in the context-independent subsequent memory effect group.

Compared to the context-independent subsequent memory effect, no activity for the context-dependent subsequent memory effect was found in temporoparietal areas associated with semantic processing (Binder et al., 2009).

5.2.3. Context-dependent versus Context-independent Subsequent Memory

To further investigate differences between context-dependent and context-independent subsequent memory, targets only remembered when the context is reinstated

(MH) were contrasted with target-items recognized independent of contextual manipulation (HH). This contrast (Enc: MH > HH) yields four clusters, two of which were located in the AIC. As expected from previous results, bilateral AIC activity was found to predict a context-dependent subsequent memory effect. To confirm this property as unique to the AIC, a conjunction analysis was performed between context-dependent subsequent memory and context-dependent versus context-independent memory (Conj: MH > MM & MH > HH). Only the two clusters located in right and left AIC remained, indicating that the bilateral AIC was the only cortical area preferentially active for context-dependent subsequent memory. These results suggest a role of the AIC in target-context-binding during encoding. In a meta-analysis of 131 memory paradigms, Kurth et al. (2010) found bilateral AIC activity to be associated with memory. Unfortunately, encoding and retrieval studies were not separately analyzed in their paper.

5.3. Neural Correlates of Contextual Processing during Retrieval

5.3.1. Retrieval 1

At this stage of the experiment two contrasts were considered to be of theoretical interest. The paradigm allowed the analysis of retrieval success independent of context while also permitting insight into context-dependent forgetting. Approaching neuronal processes causing the behavioral effect of recognition failure of recognizable words seemed possible, especially when the effect was compared to recognition success despite the presence of a changed context.

5.3.1.1. Context-independent Retrieval Success versus Forgetting

In the contrast describing retrieval success versus forgetting for context-independent items (Ret1: HH > MM), neural activity for context-independent recognition was extracted and compared to established data for retrieval success. Notably, this analysis compared target-items that were correctly recognized not only at retrieval 1, but also in a subsequent memory test. Target-items were recognizable despite contextual change and prolonged temporal distance to the encoding episode. Most studies investigating retrieval success have been using hit versus correct rejection contrasts. Participants were asked to judge whether a stimuli has been presented previously, thus comparing the activity of “old” items with items correctly determined to be “new”. Nevertheless, a similar pattern of activity was expected in a

context-independent hit versus miss contrast (Ret1: HH > MM), when retrieval success was contrasted with a target missed in two successive recognition tasks. The later target-items were assumed to be encoded either very poorly or not at all, consequently, representing context-independent retrieval failure.

Sizable clusters of activity (see table 5, p. 42) were found in both frontal and parietal cortical areas, and additional clusters in temporal and sub-cortical areas. The vast majority of frontal activations were left-lateralized in the middle and inferior frontal gyrus (BA 6, 8, 9, 11), while bilateral inferior frontal gyrus activity could be detected in BA 47. On the left side of the inferior frontal gyrus, the activity cluster seems to extend into the area of the left anterior insular cortex (AIC). Left-lateralization was predominantly also found for parietal activity in the superior parietal lobule and precuneus (BA 7). Additional parietal activations were found in the right inferior parietal lobule (BA 40).

These left-lateralized areas in the frontal and parietal cortex, as well as corresponding smaller right-sided areas, were also observed with the highest activation likelihood estimation in the review by Spaniol et al. (2009). Compared to this meta-analysis, the present study showed high concordance for frontal and parietal activity. In Spaniol's analysis for hits versus correct rejections bilateral insula activity was included in the areas sorted by activation likelihood estimation. For hits versus misses for context-independent items left-lateralized AIC activity was found. The failure to observe right-lateralized AIC activity may be attributable to a number of factors: for example, a lack of statistical power to detect a contra-lateral smaller activity cluster or lateralization of AIC activity depending on target-stimulus type (e.g., verbal versus object material). Although retrieval success was primarily measured in contrasts using hit versus correct rejections, there are studies using hits versus misses to indicate retrieval success. Henson, Hornberger & Rugg, 2005 contrasted shallow hits with shallow misses. The parietal neural activation found in their study overlaps considerably with activity found in the present study.

As suggested by Spaniol et al. (2009), frontal activity was predominately found in left middle and superior frontal gyri (BA 6, 8, 9) for retrieval 1. This area is part of the dorsolateral prefrontal cortex and has been associated with recollective monitoring (Dobbins et al., 2002) during source recollection (Dobbins & Wagner, 2005). A second activity cluster in the frontal lobe was located in the bilateral inferior frontal gyrus in the area of the ventrolateral prefrontal cortex (VLPFC; BA 47), with the left-lateralized activity cluster overflowing into the left AIC. The VLPFC has been associated with semantic retrieval (Bokde et al., 2001; Dobbins & Wagner, 2005). The anterior VLPFC (BA 47), especially, has been associated with controlled retrieval (top-down), when automatic retrieval (bottom-up) remains unsuccessful (Badre et al., 2005, Wagner et al., 2001). The left inferior frontal gyrus is also implicated in interference resolution (Badre & Wagner, 2005), being more active for interference versus non-

interference trials. A similar function was proposed for the anterior insular cortex (AIC). It was connected to both interference resolution and executive control (Wager et al., 2005; Nee et al., 2007).

Although frontal and parietal activity was mainly elicited in the left cerebral hemisphere, temporal activity was found bilaterally with a bigger cluster in the right middle temporal gyrus (BA 37, 21). Activity in the middle temporal lobe is associated with retrieval of long-term semantic knowledge (Bokde et al., 2001; Dobbins et al., 2002; Dobbins & Wagner, 2005). Activity in the middle temporal gyrus is often paired with activity in the left anterior VLPFC (BA 47), indicating successful semantic retrieval (Bokde et al., 2001, Badre et al., 2005, Dobbins & Wagner, 2005). Further activations were observed in the left basal ganglia (caudate) and right cerebellum (declive).

5.3.1.2. Context-dependent versus Context-independent Forgetting

A second analysis was conducted on context-dependent misses versus context-independent misses (Ret1: MH > MM), extracting the neural correlate of context-dependent versus context-independent forgetting (table 5, p. 42). Comparing targets subsequently retrievable when the context was reinstated (MH) with target-items that were forgotten regardless of context (MM) provided a clue as to what kind of neural events were in progress when a recognizable stimulus failed to be recognized due to context manipulation. Areas of activity were found in the left inferior (BA 47) and bilateral superior frontal gyrus (BA 8, 6) as well as bilateral AIC activity. Additional foci were located in the left parahippocampal gyrus centered on the parahippocampal cortex (PHC; BA 35) and bilateral cerebellum (culmen).

A region of interest analysis performed on selected areas according to target-item types showed two patterns of activation. While left inferior frontal gyrus (BA 47, figure 7 a, p. 44) and left PHC (BA 35; figure 7 d, p. 44) only distinguished between retrieval success and retrieval failure regardless of context, the AIC (figure 7 b, c, p. 44) was associated with context-dependent forgetting. Thus, the highest activity was found for target-items forgotten due to context change (MH), followed by targets remembered in spite of contextual change (HH) and targets missed independent of context change (MM).

To confirm these results, a contrast was calculated exclusively masking context-dependent forgetting (Ret1: MH > MM) with context-independent retrieval success (Ret1: HH > MM). Three clusters of activity became significant. As anticipated, bilateral AIC was associated with context-dependent forgetting. Unexpectedly, a third cluster in the right superior frontal gyrus (BA 6) also seemed to be associated with context-dependent forgetting versus context-independent retrieval success.

Previously, a role of the bilateral AIC in target-context-binding was proposed. At this stage of the experiment, a link between bilateral AIC activity and context-dependent

forgetting emerged. An activation of the AIC during retrieval 1 resulted in recognition failure of a later recognizable stimulus. Thus, a binding of the target to a specific context during encoding by means of AIC activity led to subsequent recognition failure when the target was presented in a new semantic context but resulted in recognition success when the original semantic context was reinstated. Bilateral anterior insular cortex is linked to proactive interference resolution (Wager et al., 2005) as well as emotional interference resolution (Levens & Phelps, 2010). Depending on task requirements, the question must be raised whether the AIC is able to resolve as well as cause interference.

5.3.2. Retrieval 2

At the last stage of the paradigm, the encoding context was reinstated leading to recognition of previously unrecognized targets. Two major contrasts were of interest for the second recognition test. The first contrast measured context-independent retrieval success versus failure (Ret2: HH > MM) and the second contrast measured the neural differences between context-dependent versus context-independent retrieval success (Ret2: MH > HH). The former contrast allowed insight into the neuronal pattern of activation for successful retrieval of target-items previously unsusceptible to context change. The encoded context was externally reinstated permitting a direct retrieval access to the encoding episode. The later contrast hinted towards a difference in target-item processing depending on previous processing operations. This stage of the analysis aims to extract differential activity for successfully retrieved targets that were previously sensitive to contextual change (MH) compared to successfully retrieved targets that were previously retrievable regardless of context change (HH).

5.3.2.1. Context-independent Retrieval Success versus Forgetting

For overall hits versus overall misses neural correlates of context-independent retrieval success versus context-independent retrieval failure (Ret2: HH > MM) may be extracted. At this phase of the experiment, the original cue was externally reinstated. The encoded context was presented with the encoded target. The majority of activations (table 6, p. 45) were found in the parietal (BA 31, 19, 7) and temporal lobe (BA 39, 21, 35, Hippocampus), cingulate gyrus (BA 31, 24, 29) as well as the frontal lobe (BA 10, 8), with considerable overlap to hits versus correct rejections activation likelihood estimations determined by Spaniol et al. (2009). Matching the present activity against a contrast published by Henson, Hornberger & Rugg, (2005) using hit versus misses, once again, common activity was found. Interestingly, when both recognition tests were considered, all of the frontal and parietal activity found in their study was also observed in the present study.

The largest cluster of activity for context-independent retrieval success versus failure at retrieval 2 (Ret2: HH > MM) was located in the medial anterior prefrontal cortex (aPFC; BA 10) as part of the medial frontal gyrus. Activity in the medial aPFC (BA 10, cluster size: 48, t(20) = 4.89, MNI (x y z): -4 60 8) was also found in the comparison between context-dependent retrieval success and context-independent retrieval failure at retrieval 2 (Ret2: MH > MM, results not presented). Activity in the aPFC has been associated with processes such as retrieval orientation (Simons, Gilbert et al., 2005), specification of the retrieval process (Dobbins et al., 2002; Dobbins & Wagner, 2005), and retrieval mode (Velanova et al., 2003). The aPFC may be divided into lateral and medial regions. Lateral aPFC has been connected with early specification stages of recollection, pre-retrieval monitoring or retrieval orientation (Rugg & Wilding, 2000) independent of target presentation or contextual detail (Simons, Gilbert et al., 2005; Simons, Owen et al., 2005). Medial aPFC is active during a later stage and is concerned with post-retrieval monitoring (Simons et al., 2008). Medial aPFC activity depends on the presentation of an external target stimulus (Simons, Gilbert et al., 2005) and is associated with automatic monitoring of retrieved information. It compares internally-generated retrieval information to externally perceived stimuli that set off the retrieval operation (Burgess et al., 2005; Simons et al., 2008).

The second recognition test was not only informative regarding frontal and parietal cortical activity but also showed typical retrieval activity in the bilateral parahippocampal gyrus areas, including the left hippocampus proper and right parahippocampal cortex (BA 35). One possible interpretation of these results may be that this retrieval activity for context-independent retrieval success versus retrieval failure (Ret2: HH > MM) was attributable to the context-word reinstatement. The BIC model (Diana et al., 2007; Eichenbaum et al., 2007) proposes that an input to the hippocampus corresponding to the encoding pattern leads to “pattern completion”. Presenting the original context with the target stimulus may induce a reactivation of the item-context-binding in the hippocampus, which in sequence may lead to reactivation of the contextual information in the parahippocampal cortex. Although target and context belong to the same group of stimuli (semantic material), and thus represent two items being presented at the same time, the effect leading to hippocampal and parahippocampal activation may be the reinstatement of the inter-stimuli association.

5.3.2.2. Context-dependent versus Context-independent Retrieval Success

The second contrast of interest at this stage of the experiment was between context-dependent and context-independent retrieval success (Ret2: MH > HH, table 6, p. 45). Correctly recognized items were contrasted according to what had happened in a previous recognition test in which the original context had been changed. The effect examined was the difference between a target earlier recognized only in a context-dependent setting (MH),

and a target-item earlier recognized independent of external context reinstatement (HH). There was no effect at the p = 0.001 level, indicating that there was either no neural difference, or a lack of power to observe it. When the significance level was lowered to p < 0.005, two clusters of activation were identified in the bilateral anterior insular cortex (AIC). A region of interest analysis performed for the bilateral AIC foci revealed that these were the only areas that remained significant after an overall ANOVA was performed. Surprisingly, in this contrast at retrieval 2, activity extracted for each target-item type did not follow earlier patterns. For targets forgotten independent of contextual manipulation (MM), the highest activity was found around the bilateral AIC, followed by targets successfully retrieved after context reinstatement (MH), and targets that remained retrievable independent of context (HH). There was no obvious explanation for this pattern. As expected from findings for encoding and retrieval 1, target-items recognizable independent of the contextual setting (HH) elicited a lower AIC activity compared to items that were recognizable only when the context was reinstated (MH). But targets failing retrieval attempts unrelated to contextual change and therefore context-target binding (MM) demonstrated the strongest AIC activity.

Given the fact that AIC activity for context-dependent hits versus context-independent hits (Ret2: MH > HH) was calculated at a low significance level, one might disregard these findings. It was nevertheless prudent to consider possible implications for the role of the anterior insular cortex in context-dependent recognition memory.

5.3.3. General Discussion of Retrieval Data

Before attempting to integrate results across all stages of the experiment, in order to understand the neuronal processes behind context-dependent encoding and recognition memory, analysis of the context-independent retrieval success effect across two successive retrieval tests presented a unique opportunity for a deeper understanding of the brain's strategic differences in retrieval operations depending on the recognition cue presented.

5.3.3.1. Interaction Analysis of Two Successive Recognition Tests

Presentation of an encoded target with a novel semantic context at retrieval (retrieval 1) compared to presentation of the original encoded context with the target (retrieval 2) represents a contextual manipulation for retrieval success versus retrieval failure across both tests.

Activity found in the first recognition test may hint on what processes were active to lead to successful retrieval despite a mismatch of encoded target and context and presented target and novel context (indirect, controlled retrieval of the target-item). Activity in the

second recognition test demonstrates a more direct retrieval of the target (automatic retrieval of the target-item), aided by a match of the cue (target and context) to the encoding episode.

When comparing two separate retrieval tests, each performed in separate sessions of fMRI scanning, an interaction effect contrasting between the first recognition test and the second test revealed the difference in cortical activity. The interaction effect of the recognition tests investigated activity between two retrieval tests taking into account only overall retrieval success (HH) versus overall retrieval failure (MM). Context-dependent targets (MH) were completely disregarded from this analysis.

Differential activity across the recognition tests (see table 7, p. 48) was largely found in the bilateral prefrontal cortex (BA 47, 9) and bilateral inferior parietal lobule (BA 40; MNI (x y z): -42 -56 54; 38 -54 52). The parietal cluster seemed to match an area associated with bottom-up attention in the theory of Corbetta and Shulman (2002). On closer inspection, the coordinates in the bilateral inferior parietal lobule were a closer match to the area associated with top-down rather than bottom-up attention to memory in the review by Ciaramelli et al. (2008). Average peaks of activity for seven contrasts focusing on top-down and bottom-up attention to memory were calculated in their review. For top-down attention to memory, the median coordinates were bilaterally found in the posterior intraparietal sulcus (MNI (x y z): left hemisphere -36, -57 42, right hemisphere 32 -57 44). The left supramarginal gyrus only (median coordinates: -50 -57 38) was associated with bottom-up attention to memory.

Corbetta and Shulman (2002) determined a role of the inferior parietal lobule in top-down attention. The attention-to-memory hypothesis by Ciaramelli et al. (2008), in particular – but also the dual attention processes hypothesis by Cabeza (2008) – propose a role of the superior parietal lobule and intraparietal sulcus in top-down attention-to-memory. The inferior parietal lobule is active if the presented cue does not directly lead to a target memory match via the medial temporal lobe. Indirect retrieval operations are necessary to successfully reactivate the encoding episode. The inferior parietal lobule initiates these additional retrieval operations by focusing top-down attentional processes on the memory task.

Returning to the present study, for retrieval 1, the presented word-pair (cue) did not match the target memory directly. Consequently, top-down attentional processes to memory were assumed necessary to retrieve the target memory indirectly. Thus, superior parietal lobe activity should be differentially increased for retrieval 1 (context-target mismatch) compared to retrieval 2 (original context-target pair), which was demonstrated in the present study (figure 9, p. 49). This result supports the proposal made by Ciaramelli et al. (2008) and Cabeza (2008) in their reviews, respectively.

The attention-to-memory hypothesis does not only include parietal areas connecting attention-to-memory, but also describes areas in the frontal cortex connected to top-down attention-to-memory. Here Ciaramelli et al. (2008) present an extension of the Component

Process Model (Moscovitch, 1992; Moscovitch & Winocur, 1995, 2002). The “strategic retrieval processes” necessary for indirect retrieval – when the presented cue does not automatically lead to the target memory – is initiated by parietal cortex areas but is executed through the ventrolateral prefrontal cortex (BA 47).

At retrieval 1, targets were re-paired with a new context, thus top-down attention may be assumed helpful to correctly remember the target from the encoding episode. The interaction analysis showed preferential activity in VLPFC during the first as compared to the second recognition test (figure 10, p. 49). One may conclude that if superior parietal cortex activity allocated attention towards additional retrieval attempts, the ventrolateral prefrontal cortex (BA 47) implemented the cue recovery processing necessary to overcome the context-mismatch. The VLPFC works at selecting the appropriate information that is needed to access the correct target memory (Ciaramelli et al., 2008). The processing of the cue might be accomplished by mental (internal) context reinstatement of the encoding context (Björk & Richardon-Klavehn, 1989). To test this theory further, activity for MM target-items should be equal in both retrieval tests. Target-items deemed as misses by the memory system in the MTL regardless of retrieval context should not lead to additional top-down attention-to-memory and initiation of cue recovery and thus additional retrieval attempts. In the interaction analysis for MM items, similar activation levels within the left ventrolateral prefrontal cortex were measured (figure 10, p. 49), supporting this hypothesis.

Supplementary evidence for the AtoM theory was provided by reaction times for retrieval. A significant difference was detected between retrieval 1 and retrieval 2. Participants took more time to reach a decision during the first recognition test, where top-down attention-to-memory was assumed necessary to successfully retrieve the correct target memory. Faster reaction times were measured for the second recognition test, where direct target memory retrieval through the medial temporal lobe was accomplished by external (visual) context reinstatement.

5.3.3.2. Medial Temporal Lobe Activity during Retrieval – BIC Model

While encoding activity did not yield medial temporal lobe (MTL) activation patterns, recognizable (HH, MH) compared to unrecognizable targets (MM) preferentially activated MTL areas during retrieval. The interaction effects across the first and second recognition tests did not yield medial temporal lobe activity. Thus, the paradigm attempting to manipulate semantic context did not cause a differential activity pattern within the medial temporal lobe for context-dependent as compared to context-independent recognition. Retrieval 1 activity for the left parahippocampal cortex (PHC) within a ROI analysis (figure 7, p. 44) also showed that the MTL was not susceptible to contextual manipulation with target presentation (ROI: MH(ret1) = HH(ret1)). Consequently, these results suggest that the neuronal processing

causing the behavioral effect of recognition failure of recognizable words did not include the MTL.

The imaging analysis at retrieval 1 yielded no MTL activity in the context-independent retrieval success versus failure contrast at $p< 0.001$ (Ret1: HH > MM). This may be due to a lack of statistical power for MTL activity at this experimental stage. Analysis of context-dependent versus context-independent retrieval failure (Ret1: MH > MM, table 5, p. 42) revealed left PHC (BA 35) activity at $p < 0.001$. Using a ROI analysis for the activity peak of this cluster (figure 7 d, p. 44), no significant difference in PHC activity was found between HH and MH targets, despite the fact that only HH targets were eventually recognized by the participant. PHC seems to activate for internal reinstatement of the context for the presented target and appears to lead to correct recognition of the target.

Hippocampus activity was not found at retrieval 1. But the first recognition test did not represent a clear cut process. Participants were asked to retrieve information about the presented target to match to the encoding episode. They were also presented with a novel semantic context that encouraged incidental contextual encoding. Recognition of the encoded target despite semantic contextual change theoretically required controlled retrieval. Activity for successful retrieval compared to retrieval failure outside the MTL matched activity patterns found in controlled retrieval paradigms (Velanova et al., 2003). An explanation for the lack of hippocampal activity at this stage of the experiment may be attributable to the presentation of a novel semantic context, competing with the already encoded context. The re-binding of target and context activity may have interfered with the encoded bound representation.

At retrieval 2, MTL activity in the left hippocampus and right parahippocampal cortex (BA 35) was found within the context-independent retrieval success versus failure contrast at $p < 0.001$ (Ret2: HH > MM, table 6, p. 45). While hippocampal activity for this experimental paradigm was only found if the context-target association had been reinstated externally during recognition at retrieval 2, PHC activity was found in the same context and different context condition. For targets susceptible to contextual change (MH) and targets recognizable independent of contextual change (HH), the PHC was equally active, indicating medial temporal lobe reactivity for recognizable targets.

The binding of item and context model (BIC; Diana et al., 2007, Eichenbaum et al., 2007) predicts retrieval activity in the hippocampus for the bound representation of target-item and context, while the parahippocampal cortex is preferentially active for processing of contextual information. In the present paradigm investigating the incidental influence of semantic context on memory, MTL activity did not differentially react to the contextual manipulation on target retrieval, but depended on what kind of cued retrieval test was used. No medial temporal lobe activity was found for the subsequent memory effect. While

successful internal reinstatement of the encoding context only activated the PHC (see table 5 and figure 7 d, pp. 42, 44), external reinstatement of context and target yielded hippocampal and PHC activity (see table 6, p. 45). Ranganath (2010, p. 134) interprets activity patterns predicted by BIC model not to be firmly constricted by any state of awareness. Instead, they support the retrieval of item and context information, “but other regions may be required in order to integrate recovered information in a manner that can guide conscious behavior,” (Ranganath, 2010; Eichenbaum et al., 2007.) In line with the Ranganath (2010) argument, while the present data suggest a role of the PHC and hippocampal cortex in successful memory retrieval, the behavioral outcome is determined by post-retrieval processing operation that may override MTL output. The question thus remains, which brain area(s) support(s) this supervisory function which eventually also causes recognition failure of recognizable words?

5.4. Neural Correlates of Context-dependent Memory – General Discussion

5.4.1. The Anterior Insula and Context

The results of this study support the role of an AIC in target-context-binding. By associating target and context during encoding, the AIC assists in creating a distinct episode that is more than the sum of its parts. During retrieval 1, a re-processing of the target within a salient novel context – also supported by the bilateral AIC – prevents retrieval of the previously presented target and leads to context-dependent forgetting (Tulving, 1984; Gardiner 1994; Sikström, 2000). During retrieval 2, the presentation of the original context-target word-pair leads to context-reinstatement and successful retrieval of the encoding episode (Tulving & Thompson, 1973; Wiseman & Tulving, 1976). Thus, retrieval failure of the presented target at retrieval 1 cannot be attributed to attentional lapse or excessive arousal during encoding. Successful recognition after context-reinstatement during retrieval 2 establishes that successful encoding and storage of the target-item in memory took place.

The greatest bilateral AIC activity during encoding was measured for targets only remembered after the encoded context was reinstated compared to target-items that were later remembered or forgotten regardless of context change. Reaction times at encoding cannot account for this difference; subsequently recognizable targets showed no difference between context-dependent and context-independent encoding, but reaction times did predict subsequent memory versus forgetting independent of contextual change.

Recognition failure of recognizable target words (first recognition test) leads to the greatest bilateral AIC activity. Reaction times for recognizable targets at retrieval 1 did not differentiate between context-dependent (MH) and context-independent forgetting (MM), they only predicted hits and misses related specifically to retrieval 1 (figure 5, p. 36). Recognition failure of recognizable words may not be explained by a difference in reaction time.

For the reinstatement of the context-target relationship during retrieval 2, a linear pattern of target-type-dependent activity at a low significance level ($p < 0.005$) for bilateral AIC surfaced (figure 8, p. 47). If the AIC played a crucial role during encoding (binding of target and context) and during retrieval failure in a different context condition (re-processing of the target within a salient novel context during retrieval 1), a new relationship among target-item type and insula activity would be expected when the original context was reinstated (retrieval 2).

This linear pattern of activity may be explained by the fact that HH targets were never dependent on a salient target-context connection for successful retrieval, HH target have been recognized independent of context in the previous retrieval test. Reinstated MH target-items were already bound together during the encoding episode. Compared to HH target-items, MH target-items have not been recognized independent of context in the previous test, instead a re-processing of the recognizable target took place. To overcome the mismatch between retrieval 1 and retrieval 2, additional processing is necessary to correctly identify an encoded context-dependent target-item word-pair. MM targets are items irretrievable by context-dependent as well as context-independent means. Assuming from the previous line of argument that context-independent recognition is more direct than context-dependent recognition, one may also assume that items irretrievable by either means necessitates the greatest retrieval processing activity in an attempt to complete the required task.

Additional insight may be gained by looking at previous memory studies that include anterior insular activity.

5.4.2. Previous Episodic Memory Studies Reporting Anterior Insula Activity

5.4.2.1. Memory-related Insula Activity

Even though medial temporal lobe (MTL) activity has been the dominating area of interest in memory research, Kurth, Zilles et al. (2010) associated the anterior-dorsal region of the bilateral insula with memory paradigms. In their meta-analysis, this region of the insular cortex is also correlated with other cognitive processes such as attention, language, speech, and working memory. To remove the overlap between cognitive tasks, a modified meta-analysis is used by Kurth et al. (2010) to isolate activity specific to memory paradigms

only. When concluding that right anterior-dorsal insula activity is the only area associated with memory, one must keep in mind that this meta-analysis did not differentiate between encoding and retrieval paradigms.

5.4.2.2. Encoding Activity

Although studies citing anterior insular cortex (AIC) activity during episodic memory encoding and retrieval are not uncommon, there appears to be a general reluctance to discuss insula activity patterns. Evidence substantiating the role of the insula comes from an encoding study using semantic and perceptual associations by Daselaar, Prince and Cabeza (2004). They constructed a paradigm that included a fixation baseline, which would enable them to investigate activations and deactivations during encoding beneficial and detrimental to subsequent memory. For a reverse subsequent memory (forgotten > remembered), they propose that activations may reflect forgotten items, reasoning that deactivations in the reversed subsequent memory effect may actually be beneficial to encoding for remembered items. Daselaar and colleges (2004) establish the left insula as an area that actually reflects activations for forgotten items, arguing that activity in this area is detrimental to encoding. A possible explanation supplied in their paper is increased arousal due to emotional stress preventing effective memorization. The results of the present study may allow the interpretation of their results from a new perspective. During their perceptual task, participants were instructed to encode a word-pair in various fonts by rating the aesthetical quality of the font together with the word-pair. At test, recombined items consisted of the same word-pair in a font originally presented with a different word-pair. In light of the present findings, an alternative explanation to excessive arousal leading to a miss might be a strong semantic contextual binding between the words themselves. This binding activity located in the insula might lead to the detrimental effect for the font-word-pair binding and consequently to a miss, suggesting that insula activity is associated with contextual binding for semantic material. This semantic binding might lead to context-dependent forgetting in specific retrieval paradigms, where the appropriate cue for the encoded context is not reinstated. In their semantic task, no contextual manipulation was conducted, thus for the reversed subsequent memory effect no insula activity is expected. It must be noted, however, that in Daselaar et al. (2004) the anterior insula activation was found only in the left hemisphere, whereas the present study obtained bilateral activation in the insular cortices.

Addis and McAndrews (2006) reported insula activity with successful encoding for relational load. By encoding triads of words with varying semantic relations (none, one, or two links), they used a paradigm to manipulate generative and relational load. If word triads were “zero-linked” (e.g. toys, lily, wool), participants had to engage differentially more in the generation of associations than for “one-linked” (e.g. games, Jewish, chess) or “two-linked”

triads (e.g. beverages, beer, milk). For relational load already available associations would lead to more binding of these associations during triad encoding. In their modulation analysis they are mainly focusing on medial temporal lobe activity for relational load (two-links > one-link > zero-link), citing a linear increase in activity for the left hippocampus. Another area showing the same positive linear pattern was the left insula (MNI: -40 11 -7). Yet again, left insula activity is linked to binding of associations for semantic material.

Further evidence is drawn from studies obtaining increased left AIC activity for increasing source confidence by Kirwan et al. (2008) and Sperling et al. (2003). Kirwan et al. (2008) created a paradigm that required participants to make animacy or size judgments about presented semantic stimuli during encoding. At retrieval, participants indicated old/new recognition confidence (item memory) on a six-point scale. For old-judgments participants also had to indicate whether they performed the animacy or size judgment during encoding (source memory) and their confidence about this decision. Activity of the right AIC and right ventrolateral prefrontal cortex (VLPFC) at encoding was associated with increased source confidence rating when item memory strength was held constant (miss; low; medium; high source memory confidence > high confidence item memory). Referring to the prefrontal activity, Kirwan et al. (2008, p. 10547) explains these results as “activity related specifically to recollective success or confidence in the recollective decision, independent of item memory strength.” Interestingly, medium confidence source memory > high confidence item memory elicited stronger right VLPFC/insula activity than high confidence source memory versus high confidence item memory.

In a paradigm where faces were presented with names, Sperling et al. (2003) asked participants in an associative task to judge whether or not they felt that these face-name-parings were a “fit”. At retrieval, they were presented with the same faces and two names for each face. Participants had to recognize the name presented with the face during encoding and indicated their decision confidence as high or low. Sperling et al. (2003) found left AIC activity for successful encoding in a contrast comparing high confidence correct recognition with recognition failure.

In a somewhat similar experiment, Ranganath et al. (2003) required participants to rate the animacy (living/non-living object) or size (object may/may not fit into a shoebox) of presented words. During retrieval, through a six-point confidence rating scale (1-6, 1 = sure new, 6 = sure old), participants evaluated their confidence that the presented item was previously studied. Participants were also asked to make a source memory judgment by indicating whether the word was studied in green (size judgment task) or red (animacy task) during encoding. In two separate contrasts, a subsequent memory effect for familiarity as well as recollection was calculated. Ranganath et al. estimated the subsequent familiarity effect by correlating encoding activity with item memory response confidence ratings (1-5),

while the subsequent recollection effect was indexed by correct versus incorrect source memory. Right anterior insular cortex activity was found for the subsequent familiarity effect measuring an increase in recognition confidence, while left anterior insular cortex activity was found for the subsequent recollection effect indicating correct source memory.

All these studies required participants to create an association between a specific context and a presented item during encoding. An attempt to integrate previous studies with the results of the present study would be by proposing that high recognition confidence and correct source memory stems from the binding of faces and names or animacy/size-word associations into specific memory traces. This binding of context and item may be accomplished by the anterior insular cortex.

5.4.2.3. Retrieval Activity

Ross and Slotnick (2008) describe bilateral AIC activity in a visual-spatial source memory design for retrieval. The anterior insular cortex was more active for correctly recognized shapes and locations (item and source memory) than for shapes recognized without correct retrieval of the location information (source memory). Simons, Owen et al. (2005) conducted an experiment using words and famous faces in combination with judgment and position tasks serving as context stimuli in their source memory paradigm. During retrieval, bilateral AIC activity as part of a larger cluster also encompassing the bilateral VLPFC was found for correct context recollection versus a baseline condition.

There is no clear story about insula contribution when episodic memory is investigated in terms of recollection and familiarity. Yonelinas et al. (2005) found activity in the left insula for remember responses in comparison to high confidence familiarity responses. During encoding, participants determined if a word is an abstract or a concrete entity. During retrieval, targets were intermixed with the same number of distracters and participants indicated for each word if they remembered the item with a specific detail from the encoding episode. In absence of specific details, participants indicated high familiarity confidence (4). Further confidence ratings were specified by participants to indicate recognized with low confidence (3), not recognized but unsure about the judgment (2) and definitely new (1). In a contrast investigating cortical activity for an increase in familiarity from 1 to 4 (new to high confidence familiarity), Yonelinas et al. obtained left AIC activity. The opposite contrast (decreasing with familiarity 4 to 1) also leads to increased insula activity, but in the left posterior insular cortex.

A similar set-up conducted by Cohn et al. (2009) found a linear increase in bilateral AIC activity for an increase in memory strength (familiarity ratings, 1 to 4) that did not include recollection. In a second contrast, right AIC activity was found when cued recollection versus cued high familiarity was contrasted and masked by memory strength.

Thus, the groups of Yonelinas and Cohn, respectively, found evidence that AIC activity correlates with subjective memory strength during retrieval. They also found that the strongest activity was elicited for recollected items (also compare: Ross & Slotnick, 2008; Simons, Owen et al., 2005). For these items, a specific contextual detail from the encoding episode was reinstated during retrieval, eliciting reinstatement activity of the context-item-association in the AIC.

Montaldi et al. (2006) performed an experiment where participants studied complex pictures and completed a perceptual task. At retrieval, participants were instructed to rate levels of familiarity (F1 to F3; very weak, moderate, and strong familiarity) and identify recollection. Several contrasts yielded insula activity, but only one cluster was located in the anterior part of the insular cortex. In contrast to Yonelinas et al. (2005) and Cohn et al. (2009), Montaldi and colleges found left AIC activity to show a linear decrease with familiarity strength. AIC activity decreased when familiarity increased.

As compared to encoding data, retrieval activity for the AIC is not uniform, indicating a purpose of the AIC in episodic retrieval that is more complex in character. The available data does not allow for a simple dissociation between recollection and familiarity for the AIC. A more general function modifying episodic memory retrieval processes must be assumed.

5.4.3. Anatomy and Connectivity of the Insular Cortex

Another approach at understanding a cortical area's functional purpose is by analyzing its anatomical structure and connectivity. Anatomical studies of insular connectivity circuits have established a connection of the anterior insular cortex (AIC) with areas in the medial temporal lobe. Augustine (1996) found afferent connections from the entorhinal cortex and efferent pathways to the perirhinal and entorhinal cortices. The main afferent connections to the entorhinal cortex originate in the anterior agranular field with fewer connections from the intermediate dysgranular field located in between the anterior and posterior (granular) sub-sections of the insular cortex (Augustine, 1996; Mesulam and Mufson 1985). The connected areas are essential parts of the medial temporal lobe supporting the declarative memory system (Moscovitch, 2000; Eichenbaum, 2006; Eichenbaum et al., 2007).

In a meta-analysis of neuroimaging studies, Kurth, Zilles et al. (2010) reveal four distinct functional areas of the insular cortex. The mid-posterior insula is preferentially activated during sensorimotor activity, while the central insula reacts to olfacto-gustatory stimuli. The anterior insula may be divided into an anterior-ventral area contributing to social-emotional processing and anterior-dorsal area active during cognitive tasks. Conjunction analysis between all domains pointed towards the anterior-dorsal insula as a multimodal

integration system. Kurth and colleges concluded that this integrative function reflects “a link between [domains] necessary to integrate different qualities into a coherent experience of the world and setting the context for thoughts and actions” (Kurth, Zilles et al., 2010, p. 519).

5.4.4. Episodic Memory Encoding and Neuronal Correlates of Awareness

5.4.4.1. “The Global Emotional Moment”

Beyond episodic memory, the insular cortex is implicated in numerous behavioral paradigms and physiological conditions. In an experiment investigating pain processing, lateralization, and attention to pain, Brooks and colleges (2002) applied painful thermal stimuli to the right and left thenar. In two experimental contexts, they examined the neuronal effect of attention on pain processing – participants focused on the pain or attended a visual distracter task. An increase in posterior insular cortex (PIC) activity was detected contralateral to the stimulus origin independent of contextual manipulation. This area appears to be a thermosensory cortex (Brooks et al., 2002; Craig et al., 2000). In contrast to the uniform activity of the PIC, activity found in the anterior insular cortex (AIC) demonstrated attentional dependency. A significant decrease in AIC activity was observed when the participant focused attention away from the pain by attending the visual task. In the distracter context, compared to the AIC, the mid-insular cortex became preferentially active. These results imply that AIC activity may be modified by attention processes (Brooks et al., 2002).

According to Damasio, consciousness is “the feeling of knowing that we have feelings” (1994, p. 285). Based on an extensive review of insula activity, Craig suggests that the insula embodies a neural correlate of consciousness (Craig, 2009a). By processing and integrating all salient incoming information, the insular cortex creates what Craig calls the “global emotional moment”. In this function the insula acts as a hierarchical sequential integration system of awareness that spans between the older PIC and the evolutionary younger AIC. Salient input is processed from basic representation of primary body function and interoception, and environmental and hedonic conditions, as well as motivational, social and cognitive conditions (Craig, 2009a).

The dorsal posterior insula represents a modality specific primary sensory cortex receiving interoceptive feelings from the whole body (Craig et al., 2000; Craig, 2009a). Comparable to the organization of the primary motor and somatosensory cortex, the PIC is organized somatotopically, but instead of a mediolateral direction (Penfield & Rasmussen, 1968), the organizational direction appears to be posterior-to-anterior (foot to mouth; Björnsdotter et al., 2009; Hua et al., 2005; Henderson et al., 2007). This primary sensory cortex spreads across the entire extent of the insular cortex in monkeys; in humans, adjacent to the primary cortex lies an integrative secondary cortex in the middle insula (Craig, 2009a).

Re-representation and integration of all primary interoceptive feelings in mid-insula are correlated with subjective ratings of stimuli quality rather than objective stimuli characteristics (Craig et al., 2000; Craig, 2010). There are hints for additional input from exteroceptive sensory sources, which may reach the mid-insula via frontal areas (Barrett & Bar, 2009; Kranczioch et al., 2005), parietal cortex (Uddin et al., 2010), and other limbic structures (Adolphs, 2002).

The culmination of representation and re-representation of all salient input in the AIC at any given time creates what we call a feeling or emotion (see Craig, 2010). The cinematoscopic succession of "global emotional moments" results in what Craig describes as the conscious representation of the "sentient self" – self-awareness. Consequently, Craig proposes that the AIC is the central component of a neural substrate that consciously represents the subjective passage of time and is uniquely involved in automatic comparisons of feelings in the present with those of the past or even in an imaginary future (Craig, 2009a; Craig, 2010).

5.4.4.2. Binding of Target and Context into the Global Emotional Moment

In light of Craig's awareness hypothesis, the interpretation of the present results suggests an expansion of the previously discussed target and context binding property of the anterior insular cortex in episodic encoding. The AIC appears to not only bind target-item and context, but consciously creates the unique episode, in Craig's words the global emotional moment, suggesting that episodic memory is the conscious content of any given moment in time. Furthermore, successful encoding of the conscious and salient content of this moment may be the beginning of episodic memory. Through the AIC's unique connectivity as the core unit of the attentional systems and its multiple connections to the medial temporal lobe memory system, it is above all suited to connect awareness to memory processes.

5.4.4.3. Neural Correlates of Awareness and Context-dependent Encoding

The presented experimental paradigm allowed three comparisons for subsequent memory effects. First, context-independent encoding success versus failure (Enc: HH > MM) yielded frequently reported encoding activity for subsequent memory paradigms. Activity (table 4, p. 38) was found around the dorsolateral (BA 9) and ventrolateral prefrontal cortex (BA 47, 45) and ventromedial prefrontal cortex (BA 11) (compare Spaniol et al., 2009). Second, context-dependent subsequent memory versus context-independent encoding failure (Enc: MH > MM) produced similar activation patterns. Additional activity for this contrast was generated by the bilateral AIC. Third, context-dependent versus context-independent subsequent memory (Enc: MH > HH) isolated bilateral AIC activity from prefrontal activity patterns. While the engagement of the prefrontal cortex distinguished

between successful encoding versus encoding failure (figure 6 a, p. 40), differentiation of context-dependent and context-independent subsequent memory occurred in bilateral AIC (figure 6 b – c, p. 40).

These results suggest that encoding of targets in a distinct contextual setting led to encoding of both the semantic target and context word into one encoding episode. One explanation may be that the saliency of stimulus and task caused a differential activity in the anterior insular cortex. In the present experiment, a medium level of activity was linked to context-independent encoding success while a high level of activity was linked to context-dependent encoding success. A low level of activity was associated with context-independent encoding failure.

This difference in activity levels across item types during encoding may have correlated with the vividness of the encoding episode, the saliency. Increased AIC activity was associated with successful encoding of items that subsequently led to context-dependent and context-independent subsequent memory. Compared to this activity level, a significantly lower activity level was associated with context-independent encoding failure. One possible explanation was that a low level of AIC activity indicated a lack of salience for the encoding stimulus and context-independent encoding failure (MM) ensued. An intermediate level AIC activity, found for context-independent subsequent memory (HH) may have aided retrieval by reinstatement of the encoded context episode. The highest level of bilateral AIC activity was detected for context-dependent encoding success (MH). This level of insular activity enabled the creation of a distinct subjective connection between target and context, previously described as binding of target and context. If increased AIC activity was associated with an increase in salience, a more and more unique encoding episode was created for the target. Furthermore, increased distinctiveness of this episode may have increased probability for later recognition failure of recognizable words, when the recognition cues at retrieval 1 (target and novel context) failed to match the encoding episode.

5.4.5. Cortical Connectivity Networks and Episodic Memory Retrieval

5.4.5.1. The Medial Temporal Lobe – Part of the Default Mode Network

By looking beyond a particular brain area's association to a cognitive behavioral function, the network approach to cognitive neuroscience may guide research by allowing it to step back in order to see a broader picture of brain function among individual puzzle pieces. Analyses of resting state functional connectivity have identified distinct cortical connectivity networks that activate and deactivate during complex cognitive tasks (Raichle et al., 2001). In the absence of goal-directed behavior in resting state imaging, or during control conditions in cognitive experimentation, a default mode network centered on the

ventromedial prefrontal cortex (VMPFC) and posterior cingulate cortex (PCC) is preferentially engaged. Additional areas considered part of the default mode network are the medial temporal lobe and the angular gyrus. A single function that engages all areas of the default network remains elusive, but individual areas of the network are associated with autobiographical and episodic memory (Kahn et al., 2008; Spreng et al., 2008), theory of mind, and self-projection including prospection – which is the act of looking into the future – (Buckner & Carroll, 2007; Spreng et al., 2008), social cognitive processes (Amodio & Frith, 2006), and semantic processing (Binder et al., 2009).

Research by Burianova et al. (2010) indicates that this network represents a common functional network for all types of declarative memory at retrieval. Sestieri et al. (2011) showed differential activation and deactivation within the DMN for memory retrieval. While the angular gyrus, posterior cingulate and precuneus were activated during retrieval, the medial prefrontal cortex was deactivated. Spreng et al (2008, p. 489) using quantitative ALE meta-analyses across domains go as far as to propose that this network is a "core network underlying a variety of cognitive domains."

5.4.5.2. The Anterior Insular Cortex and Retrieval - Mediating between Default Mode and Central Executive Network

Activity in the default mode network ceases when a salient external stimulus draws attention away from an internal resting state and onto an environmental task (Fox et al., 2005). A second cortical connectivity network is activated – key areas include the dorsolateral prefrontal cortex (DLPFC) and the posterior parietal cortex (PPC) (Menon & Uddin, 2010; Greicius et al., 2003; Greicius & Menon, 2004). Often referred to as the executive control network, it is charged with functions of goal-directed behavior such as selection and direction of attention (Eckert et al., 2009). Being concerned with maintenance and manipulation operations in working memory as well as decision-making objectives in task oriented behavior (Koechlin & Summerfield, 2007; Petrides, 2005), the network is able to initiate attention and adjust control online, also adapting to error feedback across trials (Dosenbach et al., 2007).

The central executive network seems to be one system of two seemingly distinct networks supporting attention. Eckert and colleges refer to it as the dorsal attention system, located on the lateral frontoparietal plane to separate it from the ventral attention system or salience network that includes cinguloopercular brain regions (Seeley et al., 2007; Eckert et al., 2009; Dosenbach et al., 2007). This dorsal attention system (Seeley et al., 2007) or central executive network anchored by the dorsolateral prefrontal cortex (DLPFC) is also connected to the left frontoinsula as well as frontoparietal areas that include the parietal

attention network described by Corbetta and Shulman (2002). The dorsal parietal cortex or dorsal attention system exerts top-down attention which is characterized as goal-directed and intentional (Cabeza, 2008). According to the AtoM model (attention to memory), top-down control of attention may also be applied to memory processes (Ciaramelli et al., 2008).

The ventral attention system centered on the anterior insula / frontal operculum (aI/fO) and anterior cingulate cortex (ACC) is a connectivity network that includes cortical, sub-cortical and brain stem regions. Areas in this network have frequently been associated with arousal (Fan et al., 2005). The arousal may stem from threads to homeostasis such as pain, surprise, or uncertainty. Activity in the network is task-independent (Eckert et al., 2009). Responses are the result of the “degree of personal salience” of stimuli that may be “cognitive, homoestatic, or emotional” in nature and may cause a change in affective tone (Seeley et al., 2007, p. 2349; Critchley et al., 2004; Critchley, 2005). Ensuing behavioral actions are determined by the saliency and thus significance of each stimulus to the individual, even leading to behavioral changes: “What to do (or not to do) next (Seeley et al., 2007, p. 2354)”. Frequently labeled the “salience network”, it is a third distinct cortical connectivity network among the default mode and the central executive networks (Seeley et al., 2007; Sridharan, 2008; Menon & Uddin, 2010; Bressler & Menon, 2010).

Co-activation between these networks regularly occurs for behavioral tasks including working memory, attention, and response selection (Seeley et al., 2007; Menon et al., 2001; Bressler & Menon, 2010). While the salience network recognizes relevant information from a multitude of input information, the executive control network is capable of directing and redirecting attention according to identified stimuli and homeostatic conditions. The hub connecting salience and executive-control networks was identified as the right anterior insula / frontal operculum. It is believed to initiate cognitive control systems with right anterior insula / frontal operculum activity preceding right dorsolateral prefrontal cortex activity (Eckert et al., 2009; Sridharan et al., 2008).

Menon and Uddin (2010) present a multi-step concept of anterior insula influence on task-set and cognitive control. The anterior insula may identify a salient stimulus which preferentially activates other areas in the salience network and ventrolateral and dorsolateral prefrontal cortex, initiating a bottom-up attentional switch from the default mode network to the central executive network. As a result attentional, working memory, and other cognitive resources are selectively directed to the subjectively relevant stimulus (Menon & Uddin, 2010). Consequently, activity of internally focused resting state processes decreases in favor of active processing of the external salient stimulus.

In addition to controlling the brains cortical connectivity network and attention system, the anterior insula modulates and integrates input from the autonomic nervous system through the posterior insula to adjust the body’s affective system to any salient stimulus in

order to maintain homeostasis (Craig, 2002, 2009a, Menon & Uddin, 2010). Furthermore, the strong connection between the anterior insula and anterior cingulate cortex is able to facilitate a fast behavioral adjustment including motor response to any incoming stimulus (Menon & Uddin, 2010).

Here Menon and Uddin (2010) propose a multipurpose function of the insular cortex depending on external stimuli. A variation of stimulus-induced processing may also be caused by a manipulation of presented cues during recognition memory testing. While a different-context condition requires a bottom-up attentional switch to overcome competing information between recognizable target and novel context, the same context-condition allows for automatic retrieval of encoded information.

5.4.5.3. Automatic Retrieval, Salience and Cortical Connectivity Networks

For an easier understanding of how retrieval processes are accomplished by the brain cortical connectivity networks, it is helpful to begin examining network retrieval operations for the second recognition test in the present paradigm. At retrieval 2, encoded target and context were externally reinstated, allowing for a more direct retrieval of the encoding episode.

Major activity clusters in the context-independent retrieval success versus failure contrast (Ret2: HH > MM) spanned between left medial frontal cortex housing the anterior prefrontal cortex (BA 10) and predominately left-lateralized medial parietal areas including precuneus (BA 7) and posterior cingulate cortex / retrosplenial cortex (BA 31, 29). Other clusters were found around the lateral temporoparietal junction (BA 39) and the parahippocampal gyrus, more specifically in the left hippocampus and right parahippocampal cortex. Individual areas in the frontal and parietal lobe are associated with retrieval operations. Posterior parietal cortex areas direct stimulus-driven attention to shift to or maintain attention to internally generated mnemonic representations that depend on the medial temporal lobe (Wagner et al., 2005). Medial anterior prefrontal cortex (aPFC) is associated with automatic monitoring of retrieved information (Moscovitch & Winocur, 2002), and these monitoring processes may relate to internal or external properties of context (Simons et al., 2008), as well as self-referential mental activity (Craik et al., 1999; Gusnard et al., 2001). The medial aPFC is also involved in reality monitoring (Simons et al., 2005, 2006). Posterior cingulate cortex activity for retrieval is associated with “vivid specific memories” (Moscovitch, 2005, p. 51).

The context-independent retrieval success versus failure activity found at retrieval 2 matched the activity pattern in a memory retrieval network described in a meta-analysis by Maguire (2001a) and others (Conway et al., 1999; Maguire, 2001a; Maguire, et al., 2001; Addis et al., 2004a, b). Areas in this memory network include left medial frontal cortex, left

temporal pole, left hippocampus, left anterior middle temporal gyrus, left parahippocampal cortex, retrosplenial / posterior cingulate cortex, precuneus (BA 7, middle occipital), and left temporoparietal junction (BA 40, 39; Moscovitch et al., 2005).

This memory retrieval network overlaps considerably with areas associated with the default mode network. Areas associated with the default mode network are VMPFC or aPFC (BA 10, 11), posterior cingulate cortex (BA 23, 31), MTL (hippocampus and parahippocampal gyrus) and angular gyrus (BA 39; Menon & Uddin, 2010). The default mode network is primarily associated with resting states of brain function. A resting state of brain function may not be misunderstood as serving no cognitive function but represents an automatic baseline network supporting a continuous low cognitive demand (Raichle et al., 2001; Greicius et al., 2003; Greicius & Menon, 2004). It is also associated with episodic retrieval (Cabeza et al., 2002; Cabeza et al., 2004; Sestieri et al., 2011). In summery, the default mode network represents a “conscious resting state” consisting of “retrieval and manipulation of past events, both personal and general, in an effort to solve problems and develop future plans” (Greicius et al., 2003, p. 257).

Activity in this network leads to direct or automatic retrieval of context-independent stimuli through the medial temporal lobe (Moscovitch, 1992, Moscovitch et al., 2005). This comparatively efficient retrieval operation was made possible by external reinstatement of the encoding episode during retrieval 2; the target and original context ensemble presented matched the encoded word-pair.

A second analysis at this stage of the experiment yielded information about differential neural activity between context-dependent and context-independent retrieval success (Ret2: MH > HH). Both types of target-items were correctly identified as targets by the participants, but activity patterns may have indicated preceding differences in neuronal processing. The only areas susceptible to activity difference in this contrast were the bilateral AIC (table 6, p. 45). It must be noted that activity levels for this contrast decisively differ from encoding and retrieval 1 in two important ways. First, activity levels were thresholded at a considerably lower significance level of $p < 0.005$ compared to $p < 0.001$ for the previous two phases of the experiment. If AIC activity was associated with salience of stimulus and task, retrieval 2 seemed to lack the subjective salience of encoding and retrieval 1. Second, activity levels between the different types of target-items showed a different ratio to each other. The highest level of activity was measured for targets forgotten independent of contextual manipulation in both retrieval test, followed by context-dependent targets. These target-items were missed during the first recognition test but remembered in the second. The least amount of activation was elicited by targets remembered throughout the experiment independent of context change.

At retrieval 2, all target and context words had been presented previously to the participant. Exposure to context-independent targets leading to active processing by the participant had occurred twice before. Encoding had been successful and guided recognition during retrieval 1, when targets had been correctly recognized despite a change in context. Presentation of this target-item at retrieval 2 constituted the third exposure to a well-known item. Subjective saliency of the stimulus was expected to be low. In line of this argument, a somewhat elevated level of activity was expected for successfully encoded targets, which remained unconnected to the encoding episode during retrieval 1. Through recognition failure of recognizable items at retrieval 1, the stimulus retained a certain amount of saliency. At retrieval 2, it was consciously reconnected to the encoding episode for the first time in the experimental paradigm. Finally, targets experiencing encoding failure remained unrecognized throughout the experiment. At retrieval 2, they became salient due their quality of subjective novelty among recognizable targets.

The AIC was the only neocortical area identified in this experiment that differentiated the participant's conscious knowledge of distinct items. With increased expertise, AIC reactivity decreased, indicating declining stimulus saliency. This activity pattern may have indicated a base level reactivity of AIC to external stimuli and explains the overall low level of AIC activity for retrieval 2. Task and stimuli salience during this cued recognition test (same context condition) did not require or cause the switch to attention and working-memory operations described by Menon and Uddin (2010) to increase cognitive processing power for high demanding task by activating the central executive network.

5.4.5.4. Controlled Retrieval, Retrieval Failure, Context, and Cortical Connectivity Networks

Compared to the second, the first recognition test necessitated more controlled retrieval operation to successfully remember targets. At retrieval 1, encoded targets were presented within a novel context (different context condition). The target and context ensemble presented during encoding was not externally reinstated on the screen. For retrieval of the encoded target without the original context, an indirect approach to recovering the encoded episode was necessary. The mismatch between encoded semantic context and presented semantic context during the first recognition test required additional cognitive processing to retrieve the correct target from memory.

Activation patterns (table 5, p. 42) indicated the engagement of the dorsal attention system (central executive network) to complete this task, which centered along a dorsal fronto-parietal axis. Two major activity groups were obtained. The first and strongest activity cluster in the entire experiment was found in this contrast covering the left superior parietal lobule (BA 7) and overflowing into the inferior parietal lobule (BA 40). Extensive contralateral

activity was also found for the right superior parietal lobule and a significantly smaller cluster for right inferior parietal lobule. This activity center corresponds to the posterior parietal cortex (Menon & Uddin, 2010), also described as dorsal parietal cortex (Cabeza, 2008). The second activity group was left-lateralized in the prefrontal cortex. The biggest cluster positioned on top of the left middle frontal gyrus in the dorsolateral prefrontal cortex (BA 9) and posterior dorsolateral prefrontal cortex area (BA 6). Additional small clusters were detected in bilateral inferior frontal gyrus (BA 47) spilling out into the anterior insular cortex on the left side. The central executive network (CEN) is believed to be centered in the dorsolateral prefrontal cortex, with connections to left frontoinsular and frontoparietal areas (Menon & Uddin, 2010). Activations in this fronto-parietal network suggest top-down attention to memory (Ciaramelli et al., 2008, Cabeza, 2008) in addition to engagement of selection processes and goal-directed behavior (Menon & Uddin, 2010).

Returning to the activity pattern in the interaction analysis across recognition for context-independent retrieval success versus failure or changed versus reinstated context (compare table 7, p. 48), bilateral VLPFC including bilateral AIC activity was found. In line with the argument that targets retrievable according to the MTL should have activated controlled retrieval processing to confirm recognition in order to reconcile conflicting information presented (different context condition), external context reinstatement (same context condition) should not have engaged the CEN, but DMN instead. And indeed, ROI analysis of the frontoinsular cluster (figure 10, p. 49) indicates significantly increased activity for context-independent targets (HH) in the different context condition compared to the same context condition during retrieval 2 (ROI: HH(ret1) > HH(ret2)). To test this theory even further: if the engagement of controlled retrieval operations was dependent on input from the MTL indicating retrievable information, feedback from the MTL contesting the presence of a matching memory trace should not have led to either an increase in the CEN, signifying engagement of controlled retrieval, nor decrease in the CEN, indicating engagement of the default mode network active during automatic retrieval operations. An intermediate level of activity should have indicated that neither CEN nor DMN were preferentially engaged to retrieve encoded information. Eigenvariates of the left frontoinsular cluster (figure 10, p. 49) for targets susceptible to context-independent retrieval failure (MM) did not show a significant activity difference between tests (ROI: MM(ret1) = MM(ret2)). Additionally and in accordance with the argument, context-independent retrieval failure versus success (ROI: MM(ret1) > HH(ret2)) elicited a decreased activity in the frontoinsular cluster within the second recognition test, indicating a deactivation of an area of the central executive network in favor of the default mode network. Activity in these areas further underline the evidence for engagement of the central executive network during retrieval 1 compared to retrieval 2 and

the role of the AIC in the center of attention. The AIC is believed to initiate the switch between CEN and DMN (Eckert et al., 2009; Sridharan et al., 2008).

5.4.5.5. Recognition Failure of Recognizable Words – Examining its origins

In general, retrieval failure may be due to unsuccessful encoding, resulting in a lack of retrievable information or a problem arising during the retrieval attempt. Two common causes of such problems are an inadequate retrieval cue and interference with the retrieval operation (post-retrieval processing). In a contrast comparing context-dependent to context-independent recognition failure (Ret1: MH > MM), neural correlates of recognition failure of recognizable items were investigated. The comparison yielded activity in the prefrontal cortex, medial temporal lobe and anterior insular cortex (table 5, p. 42). Activity in the left inferior frontal gyrus (BA 47) and bilateral superior frontal gyrus (BA 8, 9) represented posterior dorsolateral and ventrolateral prefrontal cortex engagement. A region of interest analysis for the biggest cluster located in the VLPFC (figure 7 a, p. 44) predicted context-dependent versus context-independent recognition failure (ROI: MH(ret1) > MM(ret1)), but did not separate between recognizable target items regardless of current recognition failure or success (ROI: MH(ret1) = HH (ret1)).

The region of interest analysis of left parahippocampal gyrus activity during retrieval 1 (figure 7 d, p. 44) identified a cluster preferentially active for successfully encoded target-items (MH, HH) compared to items showing context-independent retrieval failure (MM). There was no significant difference between targets recognized independent of contextual change and targets vulnerable to contextual change (ROI: MH(ret1) = HH(ret1)). Increased medial temporal lobe activity seemed to predict retrieval success in general, unimpeded by the ultimate behavioral assignment. Although both MH and MM target-item types were considered “new” by the participant at that stage of the experiment, successfully encoded targets elicited an increased response in the left parahippocampal gyrus as well as prefrontal cortex. Medial temporal lobe activity in the left parahippocampal gyrus correctly predicted previous successful encoding as well as later context-dependent retrieval success.

But which brain area was associated with targets showing recognition failure of recognizable items exclusively? ROI Analysis of the bilateral AIC (figure 7 b – c, p. 44) indicated significant difference in activity between item types for retrieval 1. Targets forgotten during the first recognition test but subsequently remembered (MH) elicited the strongest AIC activity, followed by targets recognized during both retrieval tests (HH) and target-items forgotten throughout (MM).

In a word recognition paradigm, Eckert et al. (2009) demonstrated that an increase in right AIC activity was not only associated with retrieval success in challenging task conditions but also with poor word recognition performance (see p. 2535). In this experiment, during

encoding, AIC activity was associated with binding of context and target into a unique encoding episode. Increased activity indicated stronger integration of context and target, decreasing the chance of successful context-reinstatement of the encoding episode when cued by a target and novel context word-pair.

Two reasons for recognition failure of recognizable words seemed feasible – retrieval failure due to an insufficient cue, causing the behavioral phenomenon, or interference with the retrieval attempt through the retrieval episode itself. The first account indicated that presentation of the novel context with the target was not strong enough to mentally reinstate the encoding episode through the medial temporal lobe, as occurred with context-independent targets. The lack of power of the target as a memory cue was due to the unique contextual binding between the semantic context and target at encoding. The second explanation implied that cognitive processing of the retrieval episode (new context and old target) by the AIC interfered with retrieval operations – the retrieval attempt was interrupted during post-retrieval processing.

The acquired data seemed to support the second account. First, the analysis of activity in the medial temporal lobe indicated retrieval success for the context-dependent targets (MH), indicating a difference between context-dependent and context-independent recognition failure at retrieval 1 (ROI: MH(ret1) > MM(ret1), figure 7 d, p. 44). Second, the activity during retrieval 1 mimicked the AIC activity of the encoding session, suggesting a processing of the target-novel-semantic-context ensemble, as occurred at encoding. Processing of both novel context and target was ensured in two ways in the experimental paradigm. Participants were asked to read both words before deciding if the second word was among the encoded words, and the context word was placed on the same screen position as the fixation cross shown in between word-pair presentation. These measures presented a strong incentive to process the novel context word before beginning retrieval operations on the target. Third, overall activity in the context-dependent versus context-independent recognition failure contrast (Ret1: MH > MM) yielded less frontal activity and no parietal clusters. Attentional processes located in these areas did not appear to be engaged. This may have been due to a lack of statistical power for this contrast compared to the significantly increased number of events in the context-independent retrieval success versus retrieval failure contrast (Ret1: HH > MM). However parietal clusters represented the strongest activity in the context-independent recognition failure versus recognition success (Ret1: HH > MM) and should have appeared for context-dependent recognition failure (Ret1: MH>MM) if areas were active, but no hint for differential parietal activity was found in this contrast. Hence, retrieval operations seemed to be interrupted early, hinting towards interference with post-retrieval processing at an early stage favoring the second account.

A medium level of AIC activity for the presented target-novel context association seemed to aid recognition by engaging the CEN to achieve top-down attention to memory. High levels of AIC activity seemed to be contra-productive. Despite the fact that the medial temporal lobe indicated the presence of successfully retrieved information, recognition failure of recognizable words occurred. The conscious processing of the association between novel context and target interfered with the recovery of the original target-context association, interrupting retrieval processes for context-dependent target-items.

5.5. Limitations

In an effort to maximize the number of events for recognition failure of recognizable words (Miss-Hit items), the different context condition (retrieval 1) was at all times presented before the same context condition (retrieval 2). One might argue that the testing presentation of retrieval 1 and retrieval 2 could have been alternated to avoid systematic effects. Theoretically, participants may have systematically changed their mental status, for example, become more accustomed to the experimental setting or may have become more and more tired during the experiment. Participant counterbalancing and an in-between group analysis were used to exclude an influence of these effects on the experiment. Multiple studies using the recognition failure of recognizable words paradigm have investigated this theoretical problem and found no difference between groups (Glass et al., 2003; Gardiner, 1994) making influential effects on the experiment improbable.

When testing for memory effects, the hippocampus and parahippocampal region are areas included in most hypotheses. This study did not show activity related to the recognition failure of recognizable words effect in the medial temporal lobe. Semantic material is known to be unreliable in eliciting hippocampal activity (Henson et al., 2005). Visual material could have been used to show more reliable effects in the medial temporal lobe, especially during encoding.

One may argue that different test cues were used for encoding and retrieval and between retrieval tests and the resulting contrasts are thus statistically unreliable. The main contrasts showing insular activity are all within tests (encoding, retrieval 1, retrieval 2) and participants were presented with the same cues during testing. Different test cues were used only in the additional comparison between retrieval 1 and retrieval 2 examining frontal and parietal activity. To measure differences between retrieval tests an interaction analysis was used to compare attentional processes (automatic retrieval versus controlled retrieval) while minimizing between test variance.

The anterior insular cortex was not included in the original hypothesis because the insular cortex has previously been associated predominately with attention. Insular activity occurring in memory paradigms was considered incidental and thus posthoc. Only recently paradigms included a priori insular activity. All results in the present study are therefore posthoc. Most memory studies investigating the influence of context on memory have used recollection versus familiarity or source-memory versus item-memory paradigms and found medial temporal lobe activity. This study used an incidental approach of context manipulation that unexpectedly but interestingly leaded no medial temporal lobe activity but changed the spotlight from the medial temporal lobe to the anterior insular cortex, opening up a new perspective on memory encoding and retrieval.

6. Conclusion

This doctoral thesis aimed at investigating neural correlates of context-dependent episodic encoding and recognition memory. A paradigm frequently used in behavioral studies of context-dependent memory (Tulving and Thompson, 1973; Gardiner, 1994) was adjusted to requirements of functional magnetic resonance imaging to test contextual effects across two successive recognition tests. In this recognition failure of recognizable word paradigm, participants were required to associate a presented word-pair, consisting of a context and target word during study, and judge their personal effectiveness in this associative task. In the ensuing retrieval phase, participants were asked to identify target words first in a different semantic context condition (novel context word) and later on in a same semantic context condition (original context word).

At the onset, neuro-cortical areas of interest were mainly expected in the medial temporal lobe. However, as observed in other studies using the subsequent memory effect for verbal material, no medial temporal lobe activity was found during encoding (Henson et al., 2005). During retrieval, medial temporal lobe activity was identified for recognizable targets compared to targets forgotten throughout – left parahippocampal cortex activity in the different context condition and left hippocampus and right parahippocampal cortex activity in the same context condition. Analysis of these results demonstrated two properties of the medial temporal lobe. First, the medial temporal lobe engages sub-regions depending on the nature of the retrieval cue. While a novel context-target cue elicited activity in the left parahippocampal cortex only, presentation of the encoded context-target ensemble induced right parahippocampal cortex and left hippocampal activity. Second, activity in the medial temporal lobe does not predict the recognition failure of recognizable items effect, but indicates successful retrieval of encoded memory information during both recognition tests.

Instead of medial temporal lobe areas, another neo-cortical area showed robust context-dependent activity in a wide variety of contrasts during the study and test phase of the experiment – the bilateral anterior insular cortex. After an extensive review of insular literature, in accordance with other cognitive studies, the thesis proposes three functions sub-served by the anterior insular cortex within cortical connectivity networks. In the present study, all of these functions are demonstrated in one memory paradigm.

(1) According to Craig (2009a), the anterior insular cortex embodies a neural correlate of awareness. Extending this theory to memory, the anterior insular cortex creates the conscious representation of the study episode encoded into the declarative memory system. Furthermore, it creates the conscious representation of the novel context and target pair in the first recognition test.

(2) The AIC is part of a “salience network” (Seeley et al., 2007; Eckert et al., 2009), which is an attention network reacting to subjective salience of a presented stimulus. With increased exposure and conscious processing of target-items, anterior insular cortex activity decreases as demonstrated in the activation pattern of the second recognition test. Therefore, the present data supplies further evidence for the role of the anterior insular cortex as part of a salience network.

(3) The AIC at the center of the salience network causes the switch between “default mode network” and “central executive network” (Sridharan, 2008) when additional attention to memory is necessary to complete a task requiring controlled retrieval (retrieval 1; Menon & Uddin, 2010; Raichle et al., 2001). A similar activity pattern supporting this theory was found in the first recognition test and in an interaction effect analysis across retrieval tests.

Anterior insular cortex involvement was found in a multitude of contrasts differentiating between context-dependent and context-independent encoding and retrieval success or failure. Recognition failure of recognizable items appears to be an interference issue caused by the unique semantic association between target and context during encoding and retrieval. Strong contextual binding seems to encourage retrieval failure if the encoding episode is not externally reinstated. In the different context condition (first recognition test), rebinding of the target with a novel context hinders retrieval of the encoding episode through the interference caused by an above-average increase of anterior insular cortex activity due to the strong salience of the novel context and target. The mode of interference proposed here is by preventing engagement of post-retrieval processing during the retrieval attempt.

Secondary to neural correlates of context-dependent episodic memory, the set-up of two successive recognition tests allows insight into automatic versus controlled retrieval operations. The episodic retrieval activity found in this study depends on the retrieval cues presented and supports the AtoM model proposed by Ciaramelli and colleges (2008). Presentation of the encoded context and target leads to automatic (direct) recognition accomplished by areas associated with the default mode network (Raichle et al., 2001) such as aPFC (~VMPFC; BA 10), posterior cingulate cortex, medial temporal lobe areas, and the temporoparietal junction around the angular gyrus. The area of the temporoparietal junction is associated with bottom-up attention to memory (Ciaramelli et al., 2008). Presentation of a novel context with the encoded target requires controlled retrieval operations to select the correct memory from a variety of irrelevant information. The central executive network – including dorsolateral prefrontal cortex, frontoinsular and frontoparietal areas – supports controlled retrieval (Menon & Uddin, 2010). The parietal areas active are associated with top-down attention to memory (Ciaramelli et al., 2008).

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Appendices

Appendix A

The instructions given to all the participants before the experiment

Appendix B

Visual aid used during oral instructions given to all the participants prior to the experiment

Appendix C

List of all words used in the experiment

Appendix D

Raw data table by participant

Appendix A

The instructions given to all the participants prior to the experiment

Allgemeines

Der Versuch besteht aus 3 großen Blöcken. Jeder Block besteht aus jeweils 4 Aufgaben. Zwischen den Blöcken und den Aufgaben wird es jeweils eine kurze Pause geben, in denen die gleich folgenden Anweisungen noch einmal über die Gegensprechanlage wiederholt werden. Wenn sie meinen einen Fehler gemacht zu haben, lassen sie sich davon nicht aus der Bahn werfen. Bleiben sie ruhig und gelassen.

Aufgabe 1

Bei der ersten Aufgabe erscheint jeweils ein Wortpaar untereinander. Das obere Wort ist in nur kleinen Buchstaben geschrieben, das untere Wort nur in großen Buchstaben. Diese beiden Wörter sollen nun bewertet werden. Die Fragestellung lautet dabei: „Können diese beiden Begriffe leicht miteinander assoziiert werden?“ Ist ihre Antwort JA: linke Taste, NEIN: rechte Taste.

Zwischen den Wortpaaren wird eine einstellige Zahl zwischen „1“ und „9“ erscheinen. Diese sollen sie auch danach bewerten, ob die Zahl gerade (linke Taste) oder ungerade (rechte Taste) ist. Zwischen den Wörterzahlenpaaren erscheint ein Kreuz.

Die Wörter und Zahlen verbleiben nicht sehr lange auf dem Bildschirm. Es ist daher sehr wichtig so schnell wie möglich eine Entscheidung zu treffen, auf jeden Fall, so lange sich die Wörter und Zahlen noch auf dem Bildschirm befinden! Bitte entscheiden sie sich für eine Antwort je Wortpaar! Lassen sie also keine Wortpaare aus und antworten sie nicht zwei Mal. Haben sie eine Taste gedrückt, ist es nicht mehr möglich ihre Meinung zu ändern.

- **Entscheiden sie sich immer solange die Wörter auf dem Bildschirm sind!**
- **Lassen sie keines der Wortpaare oder Zahlen aus!**

Aufgabe 2

Die zweite Aufgabe beinhaltet das Überprüfen der Lösung von einfachen Additions- und Subtraktionsaufgaben. Ist die Rechenaufgabe richtig gelöst, drücken sie die linke Taste. Bei einer falsch gelösten Aufgabe betätigen sie die rechte Taste.

Während der Rechenaufgaben werden sie keine Geräusche des Kernspintomographen hören.

Aufgabe 3

Bei der dritten Aufgabe geht es darum Wörter wiederzuerkennen. Sie werden wieder ein Wortpaar auf dem Bildschirm sehen. Das untere, groß geschriebene Wort sollen sie daraufhin bewerten, ob es bei den Wortpaaren in der ersten Aufgabe dabei war („alt“). Das obere, klein geschriebene Wort ist in dieser Aufgabe immer neu. Es soll ihnen dabei helfen, sich an das untere zu erinnern. Bitte lesen sie beide Wörter, bevor sie sich entscheiden. Sind sie sich absolut sicher, dass das untere Wort bei den Wortpaaren dabei war, die sie in Aufgabe 1 bewertet haben, drücken sie die linke Taste für „alt“. War das Wort nicht dabei oder sind sie sich nicht sicher, drücken sie die rechte Taste für „neu“.

Zwischen den Wortpaaren werden sie immer ein Kreuz sehen.

- **Drücken sie nur die linke Taste für „alt“, wenn sie sich absolut sicher sind!**
- **Antworten sie immer und nur mit einem Klick pro Wortpaar!**

- **Antworten sie, wenn das Wortpaar noch zu sehen ist!**

Aufgabe 4

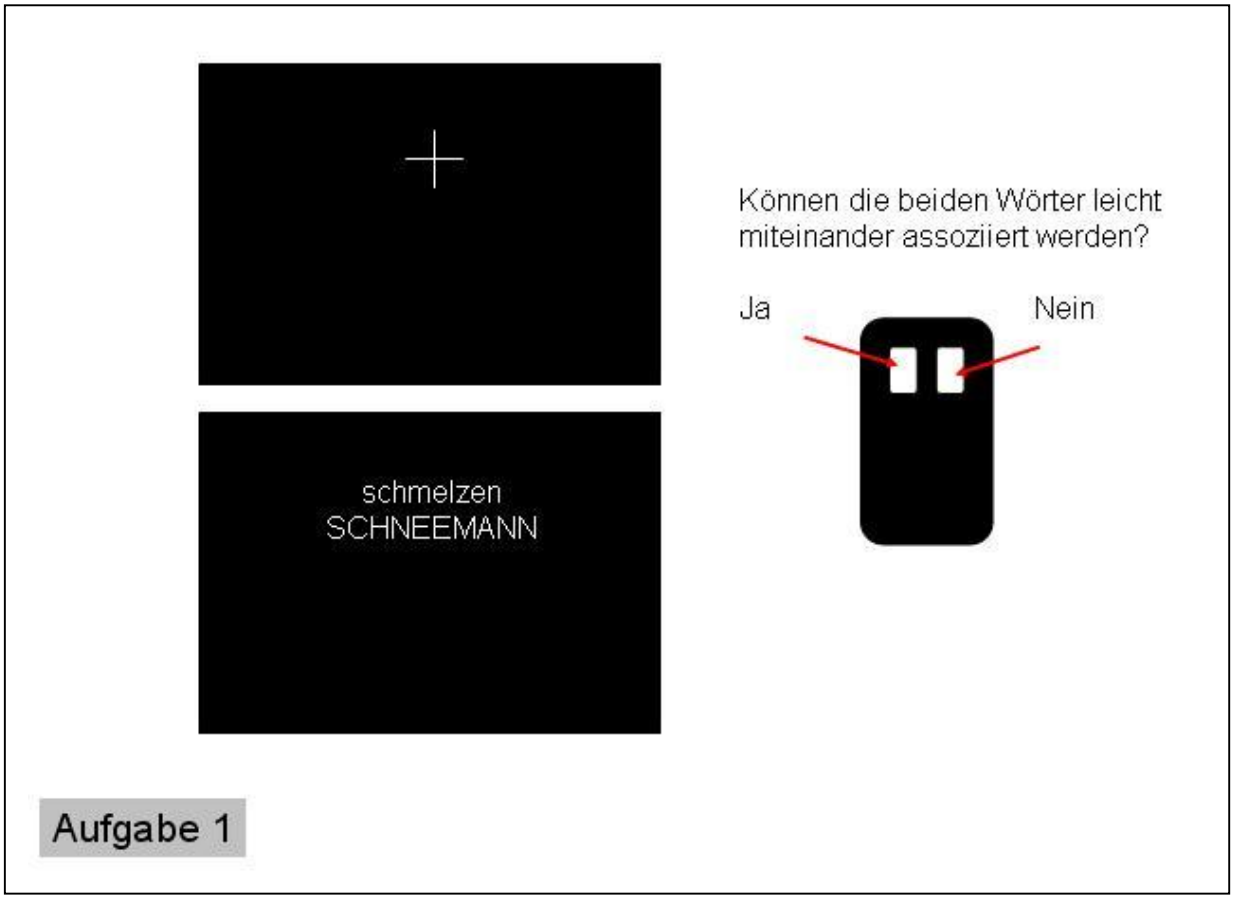
Die vierte Aufgabe ähnelt der Aufgabe zuvor. Entscheiden sie, ob das untere Wort eines der Wörter war, die sie zu Beginn des Blocks bewertet haben. Nun werden sie das untere Wort wieder in Kombination mit dem ursprünglichen oberen Wort sehen. Die Wortpaare sind die gleichen wie in Aufgabe 1.

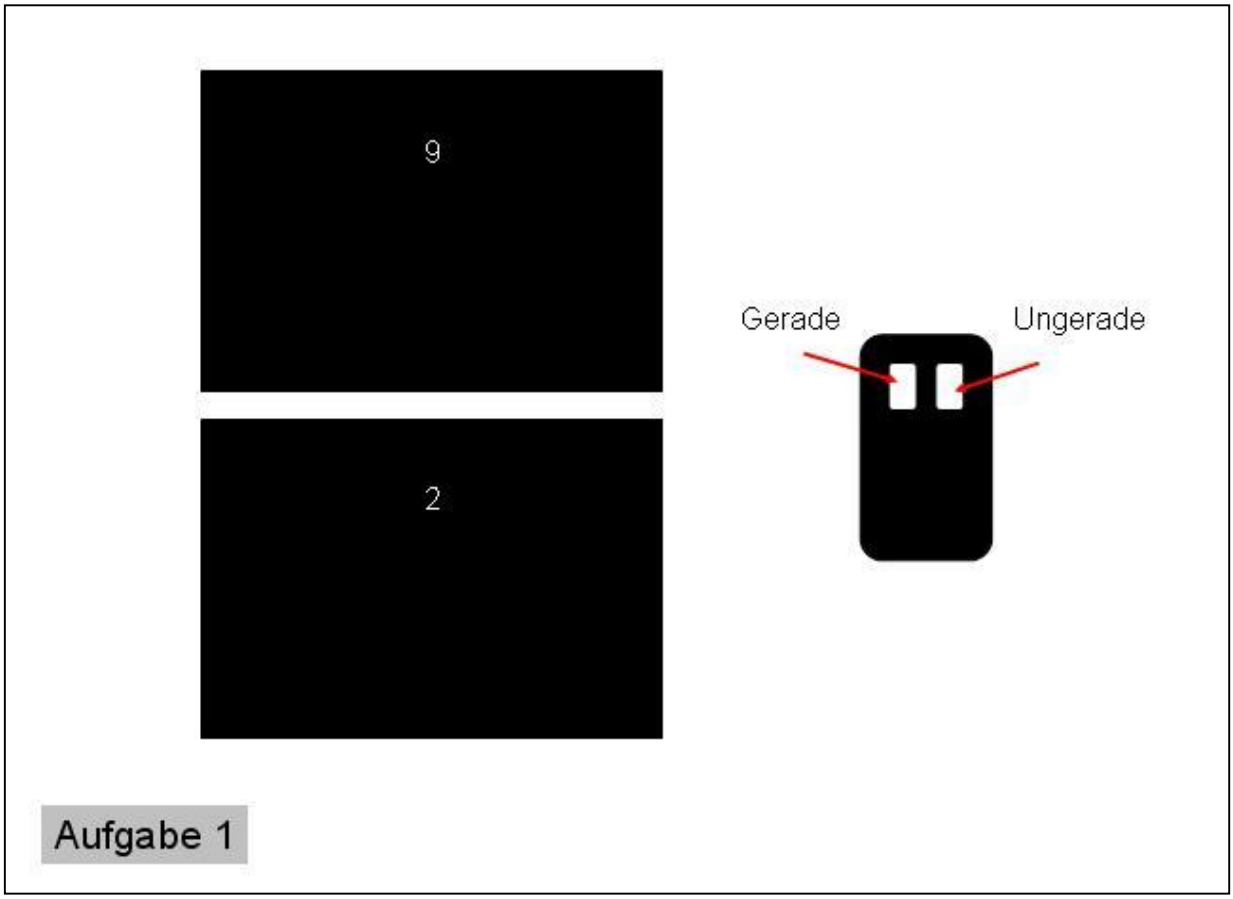
Bitte drücken sie nur die linke Taste für „alt“, wenn sie ganz sicher sind, dass das untere, groß geschriebene Wort in der ersten Aufgabe dabei war. Die neuen Wörter aus Aufgabe 3, werden auch in Aufgabe 4 die gleichen sein. Die neuen untere, groß geschriebene Wörter in dieser Aufgabe werden sie also auch schon einmal in Aufgabe 3 gesehen haben. Hier erscheinen sie jedoch in Kombination mit einem anderen oberen, klein geschriebenen Wort. Diese neuen, ihnen jedoch schon einmal gezeigten Wörter sollten sie nicht mit den alten aus Aufgabe 1 verwechseln. Nur Wörter, die auch in Aufgabe 1 von ihnen bewerten wurden, sind „alt“!

- **Bitte seien sie sich ganz sicher, wenn sie sich dafür entscheiden das untere Wort am Anfang gesehen zu haben!**
- **Drücken sie nur „alt“ (linke Taste), wenn die sich absolut an das Wort erinnern können.**
- **Bitte antworten sie immer solange sich das Wortpaar noch auf dem Bildschirm befindet!**
- **Drücken sie nur eine Taste!**

Appendix B

Visual aid used during oral instructions given to all the participants prior to the experiment

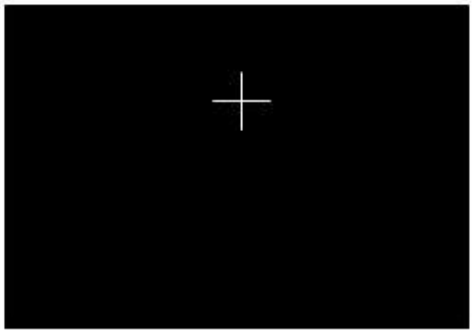




56 + 21 = 77

50 - 19 = 35

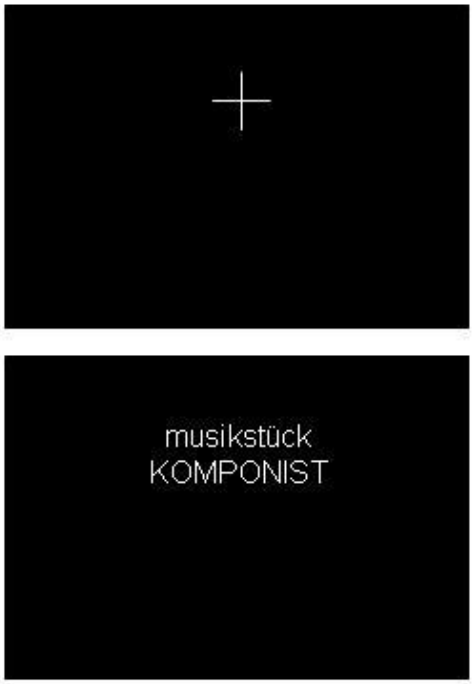
Aufgabe 2



winter
SCHNEEMANN

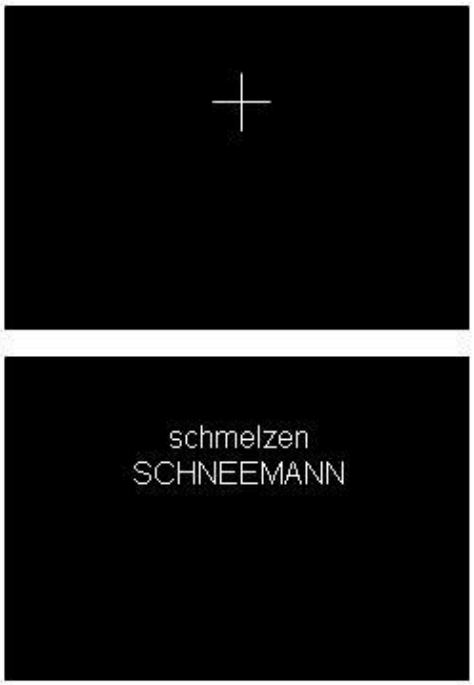
Ist WORT B alt oder neu?

Aufgabe 3



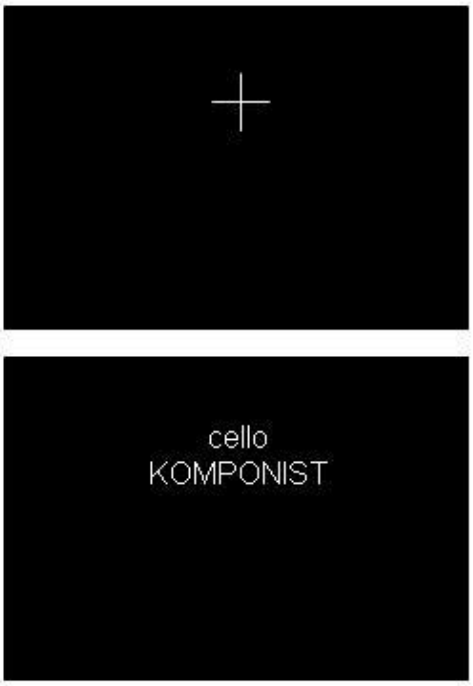
Ist WORT Y alt oder neu?

Aufgabe 3



Ist WORT B alt oder neu?

Aufgabe 4



Ist WORT Y alt oder neu?

Aufgabe 4

Appendix C

List of words used in the experiment

Strong cue	target	weak cue
einzeln	ZUSAMMEN	nahe
stück	KUCHEN	biss
tapferkeit	MUT	ritterlichkeit
blut	ROT	nadel
erscheinen	VERSCHWINDEN	verstecken
gasthaus	HOTEL	hütte
mode	KLEIDER	markt
kommunizieren	REDEN	sprache
allee	STRAßE	park
kamera	BILD	auge
mayonnaise	SENF	ei
paragraph	SATZ	aussage
feiern	PARTY	freude
stuhl	TISCH	kissen
anstrengung	VERSUCHEN	energie
bettler	BEDÜRFTIG	speise
meister	GEWINNER	läufer
papagei	VOGEL	pirat
planet	ERDE	venus
mutter	VATER	freund
alphabet	BUCHSTABE	schreiben
schicksal	ZUKUNFT	endgültig
granit	FELS	fliese
individuum	IRGENDEINER	einsam
gold	SILBER	glänzen
kino	FILM	spaß
spiegel	SPIEGELUNG	eitelkeit
gebogen	GERADE	rücken
brot	BUTTER	fleisch
stirnrunzeln	LÄCHELN	stirn
beschleunigen	GESCHWINDIGKEIT	stoppen
junge	MÄDCHEN	frau
abschießen	RAKETE	senden
wahl	STIMME	ergebnis
zirkus	CLOWN	parade
fazit	ABSCHLUSS	lösen
kalb	KUH	leber
bewundern	MÖGEN	idol
scheidung	HEIRAT	ledig
küchenchef	KOCHEN	kellner
tinte	FÜLLER	fleck
halb	GANZ	bruch
selbst	ICH	bewusst
professor	LEHRER	weise
ziegel	HAUS	holz
diamant	RING	rubin
heiligenschein	ENGEL	heilig
brise	WIND	warm
sturm	REGEN	fenster

zimmerdecke	DACH	putz
baguette	KÄSE	soße
bibel	GOTT	schule
einatmen	AUSATMEN	lunge
maultier	ESEL	ziehen
sieden	WASSER	dampf
betrag	GELD	haufen
artikel	ZEITUNG	spalte
aspirin	KOPFSCHMERZ	tablette
wortspiel	WITZ	reim
leer	VOLL	dose
fabel	GESCHICHTE	lektion
extra	MEHR	groß
aufprall	BALL	rollen
zart	ZERBRECHLICH	klein
schauspieler	SCHAUSPIELERIN	person
verloben	HEIRATEN	kennenlernen
bauch	MAGEN	krampf
köstlich	LECKER	apfel
glocke	LÄUTEN	ton
schach	SPIEL	bauer
kalender	DATUM	zeitplan
stiefel	SCHUH	leder
bar	GETRÄNK	klub
kobolt	GEIST	böse
suchen	FINDEN	fahrt
prozess	ANWALT	krawatte
holzkohle	GRILL	ruß
verweis	STRAFE	disziplin
wespe	STICH	insekt
vormund	ELTERN	erziehen
getreide	WEIZEN	samen
moor	SUMPF	dschungel
amüsieren	LACHEN	genießen
sitzen	STEHEN	still
dokument	URKUNDE	beweis
ziffer	ZAHL	rechner
dolch	MESSER	waffe
architektur	BAU	skizze
eichhörnchen	NUSS	niedlich
schloß	SCHLÜSSEL	schließen
bad	DUSCHE	handtuch
ostern	SONNTAG	frühling
gebiss	ZAHN	tier
unterschrift	NAME	berühmt
barriere	WAND	damm
bürste	HAAR	berühren
bevorzugt	BESTE	meiste
lebendig	LEICHE	gesund
schlucht	FLUSS	schildkröte
löwe	TIGER	safari
regulierung	REGEL	kontrolle
wieder	WIEDERHOLEN	jetzt
kreis	QUADRAT	linie
argumentieren	DISKUSSION	streiten

gelangweilt	MÜDE	faul
krabbeln	BABY	langsam
konzentrieren	DENKEN	zuhören
verstand	GEHIRN	erinnerung
zebra	STREIFEN	giraffe
bettleinen	LAKEN	wäsche
sinken	ANSTEIGEN	temperatur
konzept	IDEE	vision
feindseligkeit	WUT	terror
mücke	STECHEN	sommer
sterben	LEBEN	seele
netz	SPINNE	staubig
kochbuch	REZEPT	hungrig
transplantat	HERZ	änderung
schmal	BREIT	brücke
maximum	MINIMUM	sicherheit
qualität	GUT	fein
flugzeug	FLIEGEN	motor
labyrinth	MAUS	tunnel
mehrheit	MINDERHEIT	jedermann
astronomie	STERN	wissenschaftler
addieren	SUBTRAHIEREN	verbinden
kneipe	BIER	restaurant
vollenden	BEENDEN	nichts
stumm	TAUB	laut
negativ	POSITIV	gegen
glatt	FEUCHT	boden
schuldig	UNSCHULDIG	urteil
kommen	GEHEN	reisen
ausleihen	BORGEN	schulden
höhle	DUNKEL	untergrund
erreichen	ZIEL	erobern
gras	GRÜN	hof
vorne	HINTEN	führung
armee	MARINE	jacke
zuneigung	LIEBE	lust
kugel	PISTOLE	stahl
heute	MORGEN	gegenwart
richtig	FALSCH	glaube
saft	ORANGE	durst
rückwärts	VORWÄRTS	bewegung
ast	BAUM	stamm
zigarre	RAUCH	kiste
informieren	SAGEN	beraten
täuschung	LÜGE	verbrechen
samtig	WEICH	kleid
helium	BALLON	sauerstoff
medikament	HEILMITTEL	erleichterung
methode	ART	wie
klima	WETTER	schön
graben	SCHAUFEL	grund
empfangsdame	SEKRETÄRIN	angestellte
blitz	DONNER	natur
knoten	SCHNÜRSENKEL	fest
diagramm	GRAPHIK	statistik

karotte	KANINCHEN	gurke
korrekt	VERKEHRT	intelligenz
akte	AKTENSCHRANK	information
ass	KARTE	bube
füttern	ESSEN	mais
flamme	FEUER	werfen
süchtiger	DROGEN	hilflos
paar	ZWEI	zusammenpassen
antik	ALT	tempel
absurd	LÄCHERLICH	unmöglich
verteidigen	SCHÜTZEN	unterstützung
gegenstand	SACHE	spielzeug
honig	BIENE	allergie
elektrisch	GITARRE	saite
alligator	KROKODIL	see
strauß	BLUME	hübsch
kompaß	RICHTUNG	magnet
linse	BRILLE	fokus
aussterben	DINOSAURIER	spezies
gewebe	STOFF	garn
kölnischwasser	PARFÜM	spray
vanille	SCHOKOLADE	joghurt
geweih	ROTWILD	jagd
bescheiden	SCHÜCHTERN	zuversicht
erfolg	MISSERFOLG	niederlage
petersilie	GEWÜRZ	knoblauch
erwachsener	KIND	jugendlicher
blumenkohl	BROKKOLI	kopfsalat
lava	VULKAN	flüssig
vernachlässigen	IGNORIEREN	verwerfen
pelz	MANTEL	fusselig
unfall	AUTO	tragödie
kathedrale	KIRCHE	römisch
flosse	FISCH	schwanz
bizarr	SELTSAM	welt
pyramide	ÄGYPTEN	form
räuber	DIEB	maske
bibliothek	BUCH	wissenschaft
unterschiedlich	GLEICH	sonderbar
beil	AXT	säge
tor	ZAUN	klinke
zögern	WARTEN	aufschieben
braten	PFANNE	omelett
emotional	WEINEN	stress
folgen	FÜHREN	hinauf
strand	SAND	decke
turnen	BEWEGUNG	aktivität
bart	SCHNAUZER	vati
finger	HAND	gebrochen
vertrag	ABKOMMEN	gesetz
summen	SINGEN	pfeifen
geburt	TOD	krankenhaus
untersuchen	FRAGEN	erstaunen
meißel	HAMMER	gabel
aroma	DUFT	rose

atmen	LUFT	mund
kutsche	PFERD	prinzessin
bitter	SÜß	sauer
ehrlichkeit	WAHRHEIT	fair
schlafzimmer	BETT	möbel
evakuieren	VERLASSEN	erdbeben
risiko	CHANCE	furcht
angebot	NACHFRAGE	lagerung
verfolgung	LAUFEN	einfangen
gletscher	EIS	schnee
landwirtschaft	FARM	umgebung
schlafend	WACH	pause
sommersprosse	GESICHT	wange
spät	FRÜH	mitternacht
kaffee	TEE	zucker
stunde	MINUTE	später
puma	KATZE	schnell
fegen	BESEN	teppich
brennmaterial	BENZIN	antrieb
korken	WEIN	überfluten
wirbelsturm	HURRIKAN	warnung
bellen	HUND	schrei
nüchtern	BETRUNKEN	normal
anfang	ENDE	neu
ballen	FAUST	hart
richter	GERICHTSHOF	autorität
kaufen	VERKAUFEN	barzahlung
briefkasten	POST	briefmarke
ritter	RÜSTUNG	burg
deprimiert	TRAURIG	zornig
jahrzehnt	JAHR	zeitrechnung
schlacht	KRIEG	sieg
glühbirne	LICHT	rund
phantasie	TRAUM	wunsch
ursache	EFFEKT	kraft
pedal	FAHRRAD	schieben
algebra	MATHEMATIK	formel
horizont	SONNE	aussicht
fußgänger	SPAZIEREN	stadt
frieren	KALT	fest
ballett	TANZ	theater
daten	COMPUTER	analyse
aufgabe	ARBEIT	hobby
hoch	NIEDRIG	steigung
gefährte	FREUND	ehegatte
ziege	MILCH	flasche
schwarz	WEIß	mensch
uhr	ZEIT	radio
zahnbürste	ZAHNPASTA	belag
karriere	BERUF	studieren
infektion	KRANKHEIT	medizin
drucken	SCHREIBEN	seite
abreißen	ZERSTÖREN	reparieren
mikrowelle	OFEN	nuklear
limone	ZITRONE	obsttorte

frage	ANTWORT	test
künstler	MALER	schriftsteller
etikette	MANIEREN	elegant
monoton	LANGWEILIG	stimme
porzellan	PUPPE	teuer
schwach	SCHWÄCHLICH	zwecklos
mistgabel	HEU	werkzeug
pommes	KETCHUP	fett
länge	BREITE	meter
krone	KÖNIG	thron
definition	BEDEUTUNG	begriff
dünn	DICK	stock
beobachten	ZUSCHAUEN	fernrohr
lineal	MESSEN	geometrie
abschreiben	SCHUMMELN	original
neffe	NICHTE	bruder
chili	SCHARF	zunge
molekül	ATOM	winzig
auswahl	ENTSCHEIDUNG	vielzahl
führerschein	FAHRT	strafzettel
konzert	MUSIK	menge
qual	SCHMERZ	hassen
tag	NACHT	woche
verlangen	WOLLEN	süßigkeiten
anatomie	KÖRPER	frosch
brand	BOMBE	chemie
doktor	SCHWESTER	krank
dilemma	PROBLEM	katastrophe
schlechter	BESSER	nie
himmel	HÖLLE	ort
auster	MUSCHEL	roh

Appendix D

Raw data table by participant

Subject	HH	MH	HM	MM	FA1	FA2	discar.
1	111	64	10	36	9	3	22
2	137	72	9	20	6	6	2
3	94	107	4	29	0	0	8
4	121	56	23	37	7	11	3
5	128	55	13	34	3	2	14
6	131	70	6	19	5	18	24
7	34	65	13	105	1	5	32
8	105	67	18	44	7	8	6
9	110	63	14	42	5	3	15
10	115	53	14	29	5	3	33
11	180	28	7	17	8	7	9
12	164	34	9	24	5	3	9
13	126	41	13	20	3	4	41
14	106	74	18	42	6	11	0
15	96	58	18	42	13	19	30
16	87	60	37	46	7	12	13
17	150	49	12	23	7	16	7
18	53	41	38	107	4	0	1
19	109	68	24	32	8	18	4
20	89	56	40	34	12	19	29
21	92	41	39	64	2	1	5

Appendix D: behavioral raw by subject and category. Targets are categorized by retrieval success over two recognition test: HH (hit-hit), MH (miss-hit), HM (hit-miss), MM (miss-miss). Distracters falsely endorsed as targets (FA) are counted separately for each recognition test. Items discarded from the analysis due to no, multi or out-of-time responses are recorded in the last column.

Ich erkläre, dass ich die der Medizinischen Fakultät der Otto-von-Guericke-Universität zur Promotion eingereichte Dissertation mit dem Titel

Neural correlates of context-dependent memory: The role of the insula in episodic encoding and recognition memory – an fMRI experiment

In der

Klinik für Neurologie
Medizinischen Fakultät
Otto-von-Guericke-Universität Magdeburg

mit Unterstützung durch

Prof. Dr. Alan Richardson-Klavehn
Dr. Gerasimos Markopoulos

ohne sonstige Hilfe durchgeführt und bei der Abfassung der Dissertation keine anderen als die dort aufgeführten Hilfsmittel benutzt habe.

Bei der Abfassung der Dissertation sind Rechte Dritter nicht verletzt worden.

Ich habe diese Dissertation bisher an keiner in- oder ausländischen Hochschule zur Promotion eingereicht. Ich übertrage der Medizinischen Fakultät das Recht, weitere Kopien meiner Dissertation herzustellen und zu vertreiben.

Magdeburg, den 01.08.2013

Unterschrift

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